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Archives of Neurology and Psychiatry

VOLUME 25 MAY, 1931 NUMBER 5

PINEALOMAS *

JOSEPH H. GLOBUS, M.D.
AND
SAMUEL SILBERT, M.D.
NEW YORK

Tumors of the pineal body, or more correctly tumors in the region of the pineal body, are a constant challenge to both the clinician and the morphologist. The former, well prepared as he is to localize lesions in this region and successful as he may often be in identifying the character of a lesion in this location, is nevertheless much disturbed by his inability to do so in every instance. He is in constant search of diagnostic means for an early recognition of expanding lesions in this region. Unfortunately, his efforts in this direction are often blocked by the coexistence of signs and symptoms provoked by secondary alterations in parts of the brain distant from the lesion in the pineal region. Tumors in this location, which overlie and usually compress the aqueduct, are in the most favorable place for the production of obstructive hydrocephalus. The third ventricle, which is situated anterior to the obstructive lesion and is frequently invaded by it, shares in the ventricular distention. Because of this the structures in the direct vicinity of the third ventricle, such as the tuber cinereum and the hypothalamus with their important nuclei, are all affected by the rising pressure in the ventricular system. In this manner a series of signs and symptoms may arise from disturbance of the vegetative centers in the floor or walls of the third ventricle. They may become part of the clinical picture, which may be incorrectly ascribed entirely to the more obvious lesion in or about the pineal body.

In the attempt to discover a probable relationship between the morphologic alterations in the pineal region and the disturbances in the vegetative function the clinician faces the old problem of the function or functions of the unaltered pineal body. To solve this problem he must first establish the normal histologic structure of this organ, following it through its formative stages as well as through its involutional phases. He must decide whether the pineal body has ever had the

* Submitted for publication, June 11, 1930.

* From the Neurological Service and the Laboratories of the Mount Sinai Hospital.

*Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 9, 1930.

structure and functions of a true gland of internal secretion, and if so, whether it maintains them throughout the life of the person. It is obvious that on the answer to these questions will depend the interpretation given to the clinical manifestations which, though contemporary with the progressive development of a lesion in the region of the pineal body, may not be caused by it. This highly important phase of the problem could not be made part of this study, for we realized that the material at our disposal was too meager to permit conclusions as to the functions of the pineal "gland." It was also thought that no data, no matter how unimpressive, should be left unrecorded, as they may have intrinsic value for the ultimate solution of the problem.

On the other hand, the neuropathologist is often puzzled by the unusual architecture and by the great variability in structure peculiar to tumors in this region. The essential difficulty has been an inability to find some basic histologic feature that might serve in the identification of the character of such tumors. The classic contributions of Marburg,[1] Krabbe,[2] Tilney and Warren,[3] followed more recently by the studies of Horrax and Bailey,[4] have shed much light on the histogenesis of the pineal body and on the histologic character of tumors presumably derived from that organ. But there are still many obscure morphologic features that demand elucidation. The variability in structure is so great that many previous attempts to assemble tumors in this location into a single morphologic group have failed. This is apparent from the great variety of names under which the so-called pineal tumors have been recorded, though they all form in the same location and probably have a common source of origin. Haldeman,[5] going as far back as 1800, was able to collect from the literature 113 cases reported as pineal tumors, and one is struck by the great assortment of names employed to designate them. In this list one finds pineal tumors designated as fibroma, psammoma, psammosarcoma, sarcoma, glioma, gliosarcoma, carcinoma, adenoma, adenocarcinoma, neuroglioma, neuro-epithelioglioma and, finally pinealoma, pinealoblastoma and several other names.

Krabbe's [2] important contribution, in which he suggested the name pinealoma, opened the way for a more logical approach to the study of this type of tumor. Horrax and Bailey [4] and others brought forward additional information, paving the way for a more thorough under-

1. Marburg, Otto: Zur Kenntnis der normalen und pathologischen Histologie der Zirbeldruese, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **17**:217, 1908.

2. Krabbe, K. H.: Histologische und embryologische Untersuchungen über die Zirbeldruese des Menschen, Anat. Hefte **54**:191, 1916.

3. Tilney and Warren: The Morphology and Evolutionary Significance of the Pineal Body, Am. Anat. Mem. **9**:7, 1919.

4. Horrax, Gilbert; and Bailey, Percival: Tumors of the Pineal Body, Arch. Neurol. & Psychiat. **13**:423 (April) 1925.

5. Haldeman, Keene O.: Tumors of the Pineal Gland, Arch. Neurol. & Psychiat. **18**:724 (Nov.) 1927.

standing of neoplasms in this group. Unfortunately, some confusion was left in the wake of Horrax and Bailey's publications, in which they suggested the existence of glioblastic elements in tumors of this type, by proposing for some of them the term "spongioblastic pinealoma." In doing so they not only diverted a direct lead in the interpretation of the histogenetic features of such tumors, but opened up the much debated question as to the existence of gliogenous elements in the developing pineal body.

It is the common experience of almost every neuropathologist to be intrigued by the striking histologic picture of the first pinealoma coming under his observation, and then to be puzzled by the manifold variations in the histologic pictures presented by a subsequent series of tumors found in the same location and obviously of a similar origin. This divergence in histologic organization is so great that to find some basic feature that would establish their common origin seems at first to be a hopeless task.

This was the difficulty that we had to surmount in order to establish the identity of the tumors in our seven cases. To do this we found it necessary to familiarize ourselves first with the progressive and regressive changes which the pineal body undergoes in the course of its evolution from early incipiency to full maturity, and beyond that through its involutional phase. Such a study, we believed, would help to find the reason for the variability in the histologic character of the tumors, no matter how far the structural features of some may depart from the classic architecture of the typical pinealoma. It was the feeling that tumors in this location may be traced to embryonal rests that may recapitulate any of the stages in the development of the pineal body and thus assume histologic characters paralleling any phase in the life history of the gland that led us to choose this method of approach. In this way we hoped to find a basic morphologic pattern that would link all tumors in the pineal region, no matter how divergent their gross or histologic appearance.

MATERIAL AND METHODS

Material.—

A. Pineal bodies of nine fetuses of the following ages:

5½ months	1
6½ months	2
7 months	3
7½ months	2
8½ months	1

(delivered as premature 7½ months' fetus but lived thirty days)

B. Pineal bodies of eighteen infants in the first month of postnatal life:

At birth	1
1 day	1
3 days	1
5 days	1
8 days	1
12 days	1
14 days	1
15 days	1
19 days	2
20 days	1
21 days	4
22 days	1
23 days	1
24 days	1

C. Pineal bodies of twenty-five infants and young children between the ages of 1 month and 2½ years:

6 weeks	1
2 months	2
3 months	2
4 months	2
5 months	4
6 months	1
6½ months	2
8 months	1
9 months	2
10 months	2
13 months	1
15 months	1
18 months	1
24 months	1
30 months	1
5½ years	1

D. Pineal bodies of twenty-two older persons ranging up to the age of 72 years.

E. Seven tumors in the pineal region and pineal bodies in three of these cases.

A total number of seventy-seven pineal bodies was studied.

Methods.—All material was fixed in formaldehyde. Each gland, whenever possible, was cut in two; one-half was embedded in paraffin, and the other was used in the preparation of frozen sections. This, of course, could not be carried out in the very young and fetal pineal bodies. The latter were embedded in toto in paraffin. The tumor material was treated in a similar way: Paraffin and frozen sections were prepared for histologic study. The stains employed were: hematoxylin, hematoxylin-eosin, iron-hematoxylin, van Gieson, the Globus modification of Cajal's stain, the Hortega silver impregnation method for glia and the Bielschowsky method. Many of the glands, particularly the fetal and early postnatal, were cut and studied serially.

HISTOGENETIC PHASES OF THE HUMAN PINEAL BODY

Our material, as already indicated, does not include the earliest stages in the development of the pineal body, as the youngest pineal gland in our collection is that of a fetus at 5½ months. To complete the life history of this organ we have borrowed and shall give in brief the observations recorded by Krabbe and Tilney and Warren on the developmental processes in the pineal body covering the period from the earliest appearance of its anlage to about the sixth month of intrauterine life.

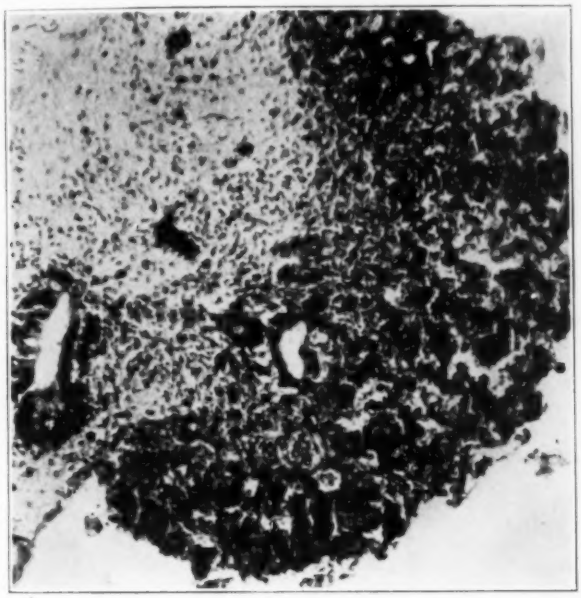

Fig. 1.—Pineal bud in fetus at 5½ months. Hematoxylin-eosin; × 50.

Krabbe noted the appearance of the anlage of the pineal body at the beginning of the second fetal month. At this time it consists of two parts: a cellular mass, and a fold posterior to it in the roof of the diencephalon. Somewhat later, the two anlagen fuse, the pineal recess deepens, its wall thickens and the cell mass enlarges. During the second month, the cells lining the pineal recess show no cilia. The cells in the anterior pineal mass are round and show no alveolar or tubular arrangement, and no blood vessels are present. In the third fetal month, the cells lining the recess show a greater amount of protoplasm and the nuclei are displaced to the base. These cells now show a cuticle and cilia on their free surface. At this time the first signs of vascularization of the cell mass appear, as seen in the

development of capillaries. The size of the cell mass continues to increase and the diverticulum deepens and narrows. In the fourth and fifth months there is an increase in the number of cells and blood vessels. The diverticulum becomes still narrower. At the end of the fifth month, the entire pineal anlage measures about 2 mm. The pineal recess is now closed, forming a cavity instead of a diverticulum. The anterior and posterior anlagen are completely fused.

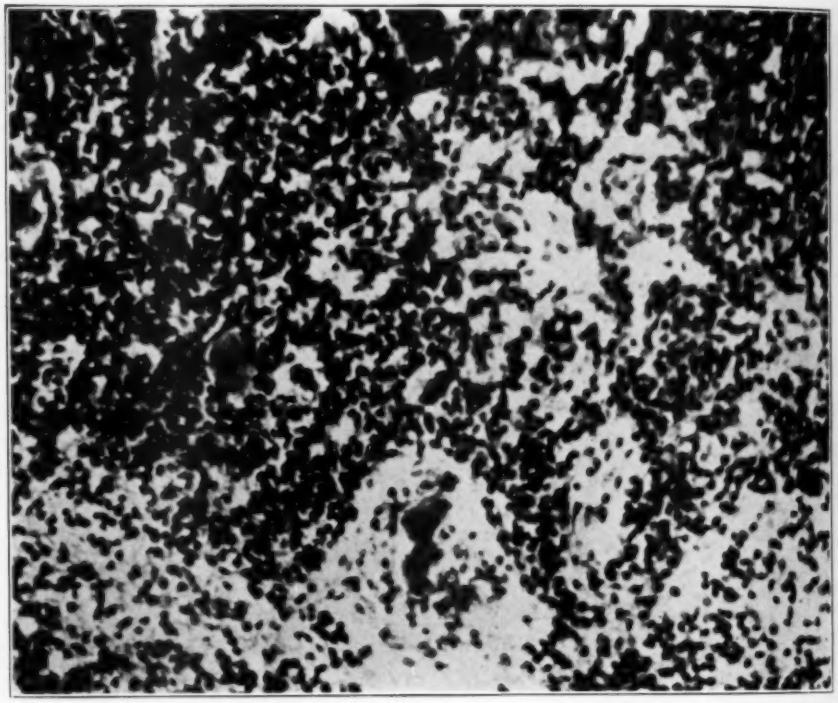

Fig. 2.—Section of pineal body of fetus at 6½ months, illustrating the process of vascularization. Hematoxlin-eosin; × 210.

In our study of developmental changes in this organ, we began with observations on its structure in a fetus at 5½ months. At this age the pineal body assumes the appearance of a fairly large bud and presents histologic features of a primitive glandular structure (fig. 1). At the rostral end of the bud several large tubules form the vanguard of a large aggregation of smaller tubules. The former are wide open and irregularly branched and are lined by columnar epithelium, while the latter are lined by cuboidal cells. All of the tubules stand out as dark-staining cellular masses on a light background, which consists of cellular elements forming a meshwork simulating embryonal supporting tissue.

The next definite structural alteration is noted in the pineal body of a fetus at 6½ months. Here, masses, which assume in places the character of solid cords of densely stained small cells, encircle the clearer zones populated by a few faintly stained cells. The latter are invaded by vascular channels (fig. 2). This is the process to which Tilney and Warren refer as the process of vascularization. Here, the first suggestion of the mosaic architecture, which will typify the late prenatal and postnatal developmental stages, becomes apparent.

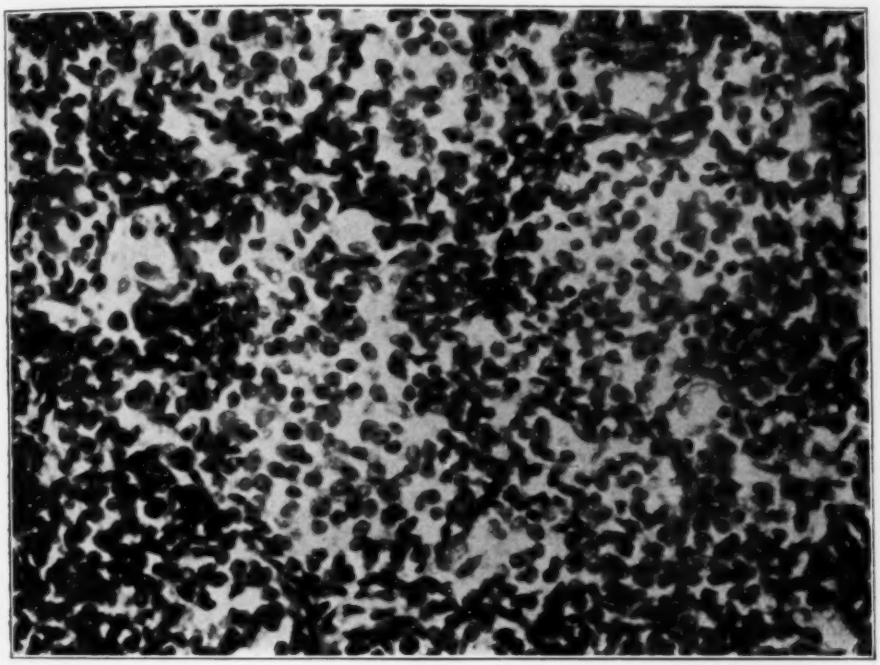

Fig. 3.—Section of pineal body of fetus at 7½ months at birth, who lived one month after delivery. Hematoxylin-eosin; × 210.

In the fetus at 7 months the so-called clear areas show an increase in the number and size of the cells in the clearer zones, and the vessels, which were prominent in the previous stage, are somewhat less conspicuous and are now displaced to the periphery of this zone.

In the 8½ month fetal pineal body another phase in differentiation becomes apparent. The pattern that will typify the structure of this organ during the late prenatal and early postnatal life comes into view. Streams of small round cells, poor in cytoplasm and with deeply staining nuclei, break up the pineal territory into irregular squares or pentagonal areas, which are populated by cell masses of lesser density and of less intense staining qualities (fig. 3). The latter are easily

distinguished from small dark cells in the encircling streams by their lighter appearance and by the large size of the individual cells. The large cells already in this stage of development show features simulating those of the mature parenchymal cells of the adult pineal body.

The last days of fetal life and first few days of postnatal life are marked by further striking alterations in the histology of the pineal

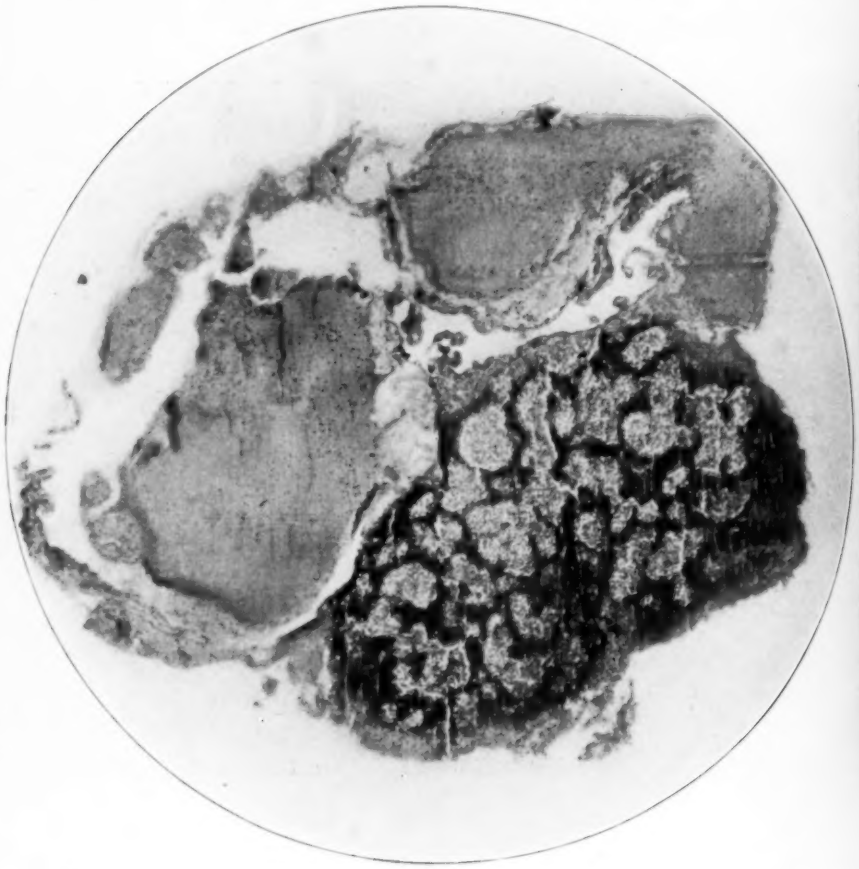

Fig. 4.—Cross-section of pineal body of an infant, aged 1 day, illustrating the characteristic mosaic and the large vascular channels at the periphery. Hematoxylin-eosin; × 50.

gland. Even under a low magnification, the characteristic pattern of clear areas surrounded by narrow zones or bands of deeply staining cellular elements becomes more apparent (fig. 4). At the periphery of the pineal body there are seen large, distended blood channels, which give the appearance of massive hemorrhages. The large vessels recall a similar picture in the development of a gland of internal secretion.

Aschoff [6] called attention to the presence of hemorrhages in the suprarenal in the early stages of postnatal life. This serves to indicate a similarity in evolutional features between an organ of internal secretion (suprarenal) and a structure with unestablished physiologic activity.

At the end of the third week in postnatal development of the pineal body, the pattern already mentioned reaches its highest stage of development (figs. 5 and 6). Here there is no apparent diminution in the number of the small cells, but the large cells have increased in size and pos-

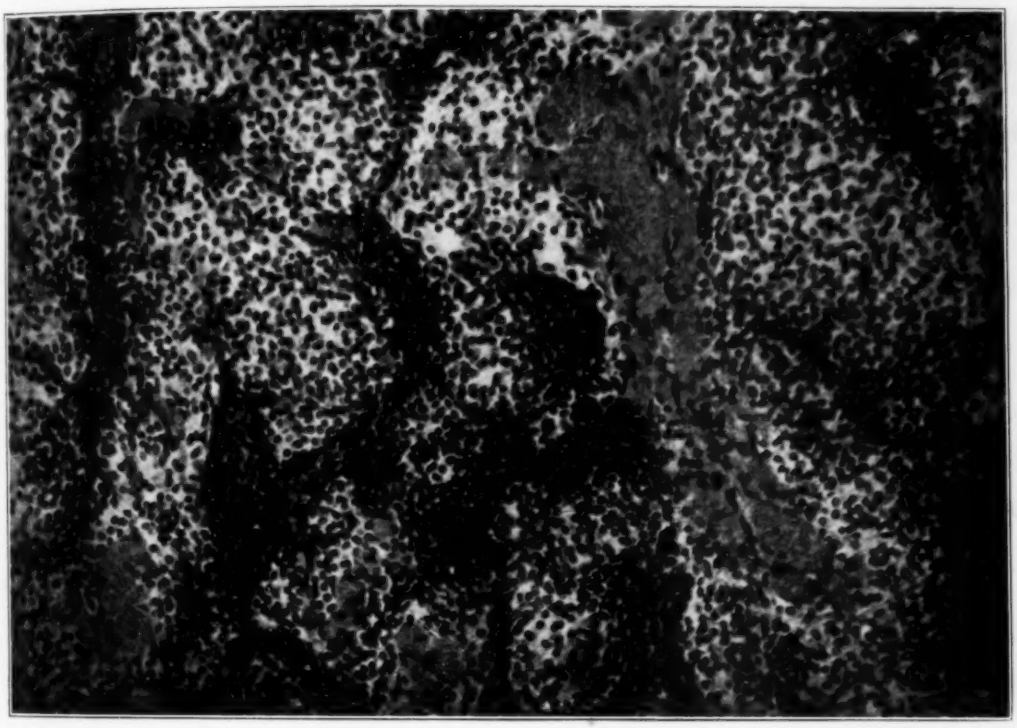

Fig. 5.—Section of pineal body of an infant, aged 19 days, showing the two cell types arranged in the characteristic mosaic. Hematoxylin-eosin; reduced from a magnification of × 250.

sibly in number. It is interesting to find that the blood vessels here are mainly in the clear parenchymal areas. The relation of blood vessels to the large cells is another feature suggestive of the glandular character of this organ.

At the end of 4 weeks of postnatal life, no further striking changes are observed (fig. 7). From this time on, however, a series of new

6. Aschoff, Ludwig: Lectures on Pathology, New York, Paul B. Hoeber, Inc., 1924, p. 101.

developmental stages begins to appear. It is already seen at the end of 9 weeks when the mosaic character of the structure begins to lose its outspoken character. The small cells begin to break up the continuity of their streamlike formation. They diminish in number (fig 8). This is still more pronounced at the end of 4 months (fig. 9).

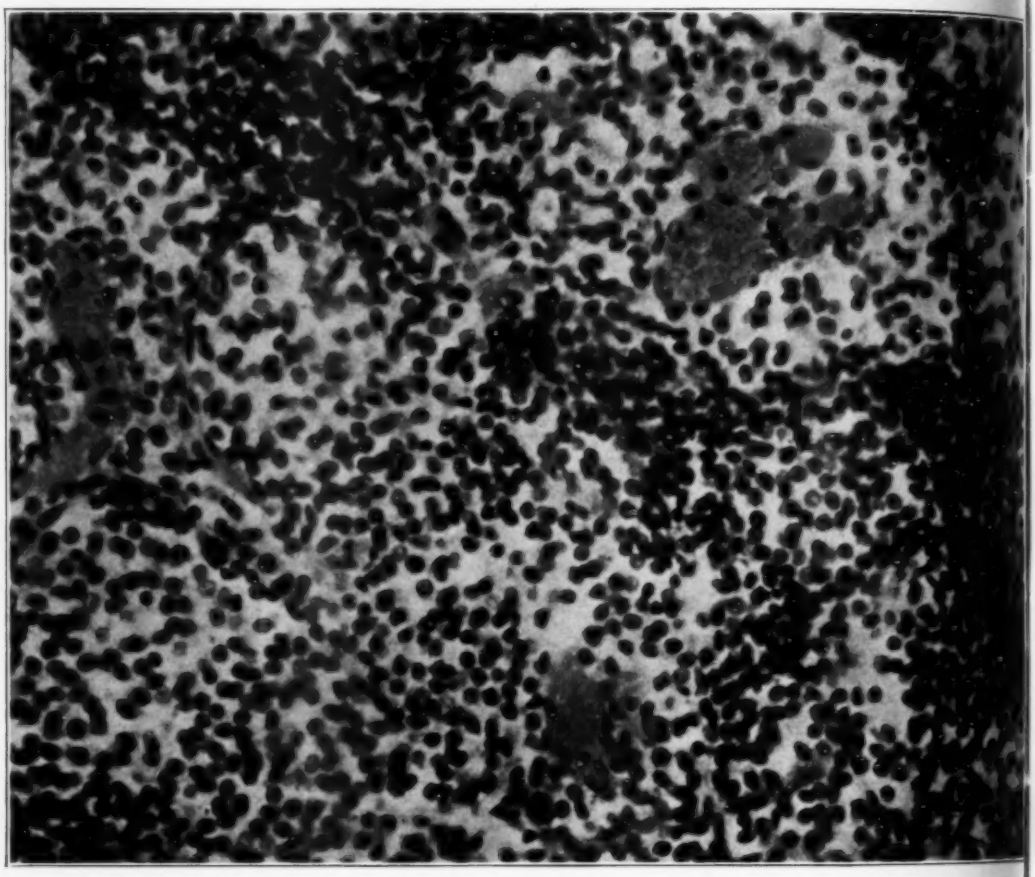

Fig. 6.—Higher magnification of the section of the pineal body shown in figure 5 to show the character of the parenchymal cells. Hematoxylin-eosin; × 400.

At the end of 5 months only small islands of the dark cells are in evidence. They assume a new character, becoming elongated, and are being transformed into fibroblasts. This is demonstrated not only by their newly acquired form but also by their staining reactions (fig. 10).

At the end of 9 months little is left of the old mosaic structure. The dark cells are now found in exceedingly small groups with here and there a few isolated cells suggesting the previous existence of large accumulations.

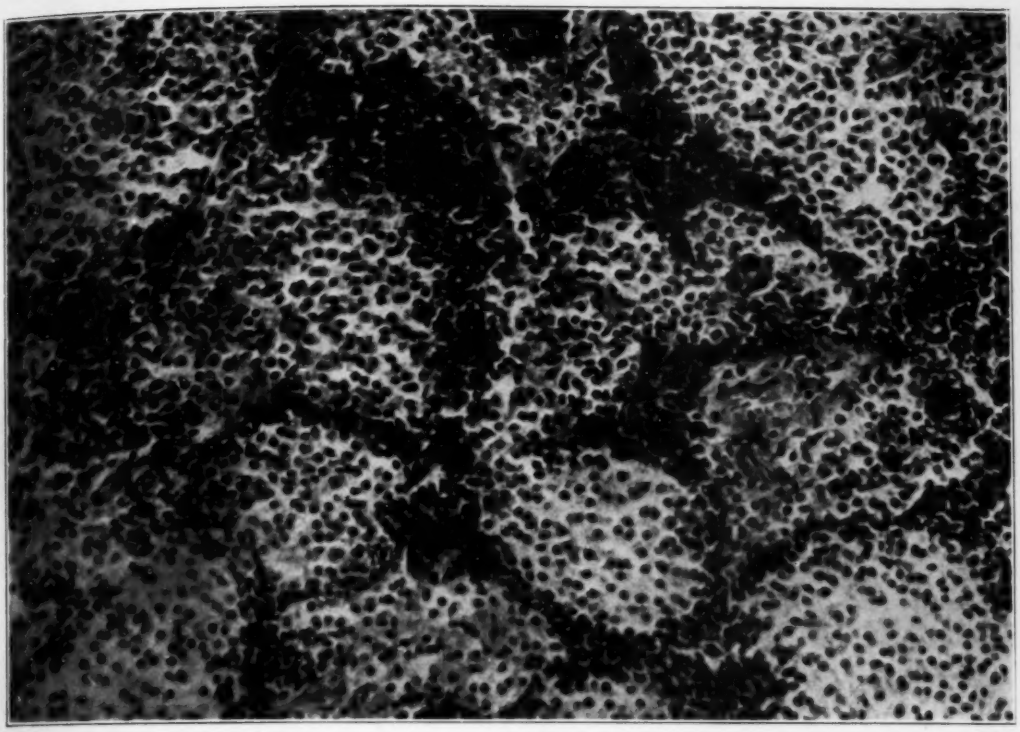

Fig. 7.—Section of pineal body of an infant, aged 28 days, still showing the typical mosaic arrangement of the two distinct cell types. Hematoxylin-eosin; reduced from a magnification of × 260.

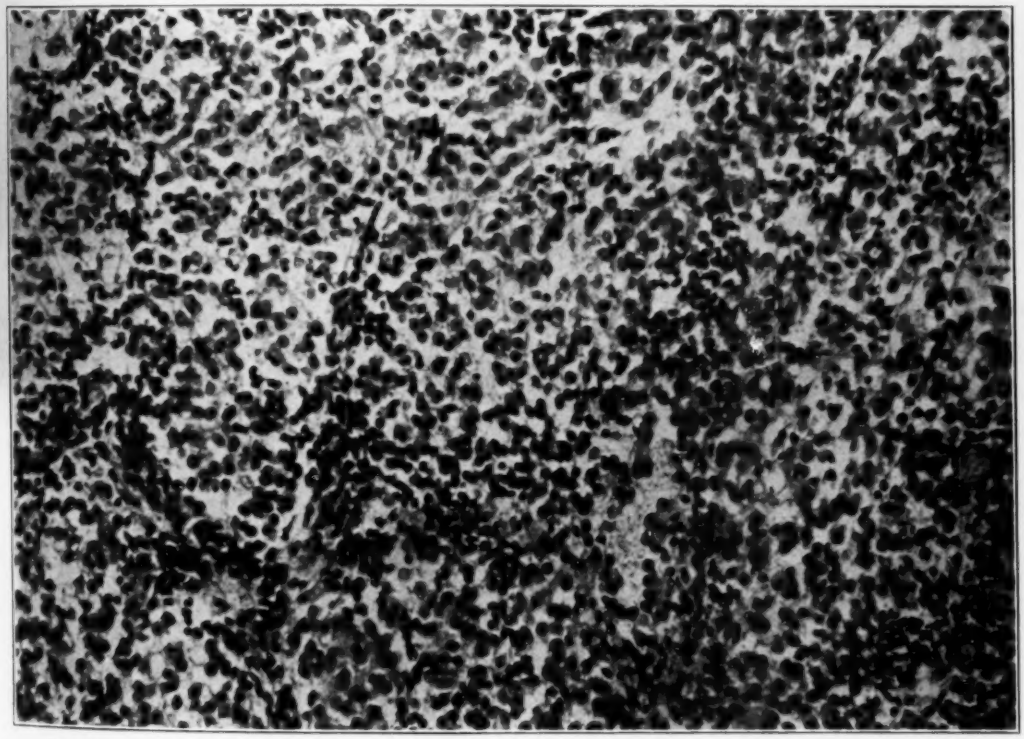

Fig. 8.—Section of pineal body of an infant, aged 9 weeks, illustrating the gradual loss of the mosaic arrangement through a decrease in the number of the small dark cells. Hematoxylin-eosin; reduced from a magnification of × 230.

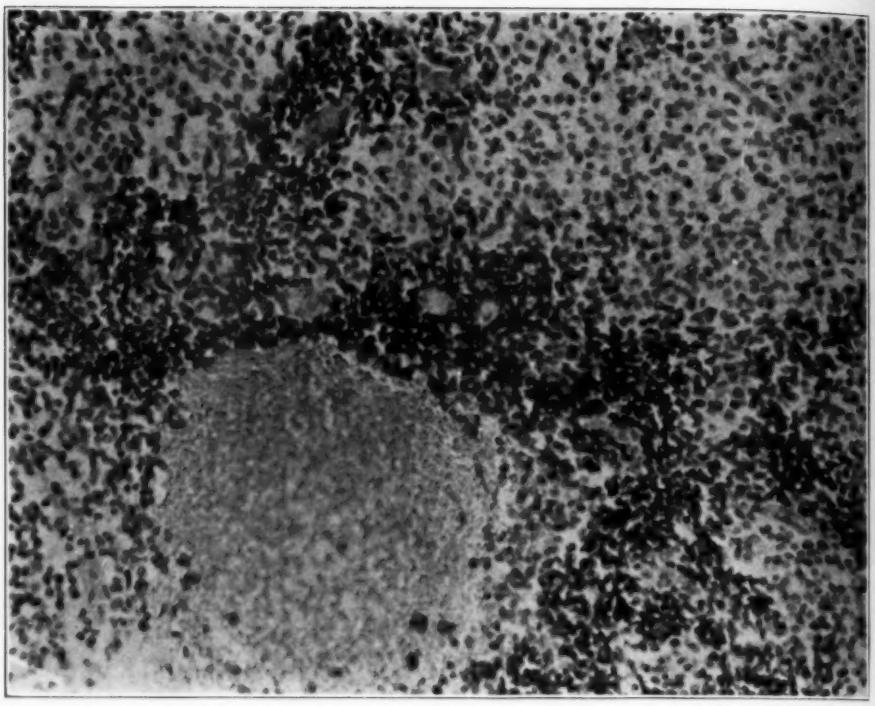

Fig. 9.—Section of pineal body of an infant, aged 4 months, showing further disappearance of the characteristic mosaic. The small cells now form isolated irregular aggregations. Hematoxylin-eosin; × 210.

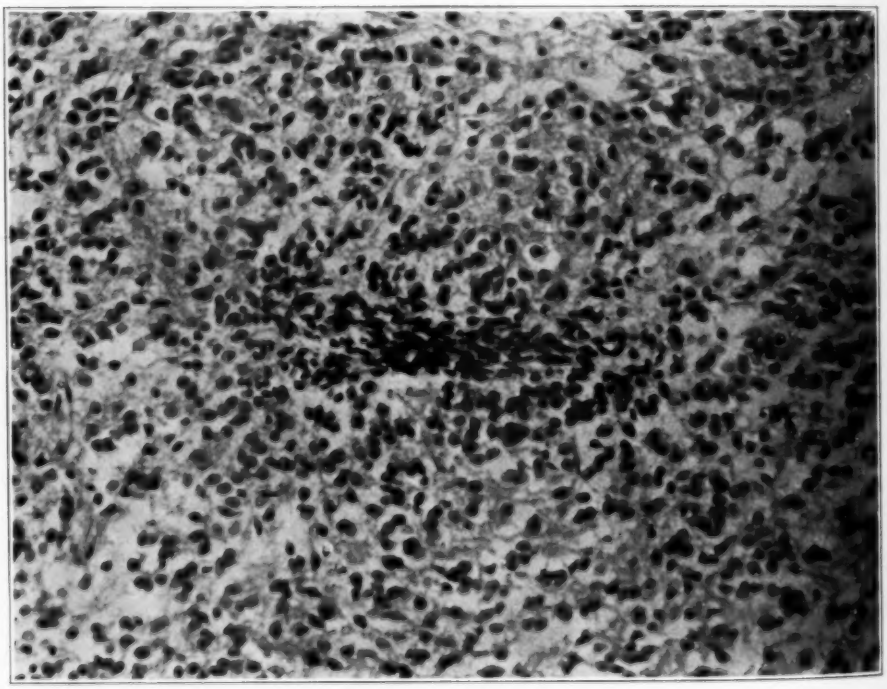

Fig. 10.—Section of pineal body of an infant, aged 5 months, showing transformation of the small dark cells into fibroblasts. Hematoxylin-eosin; × 240.

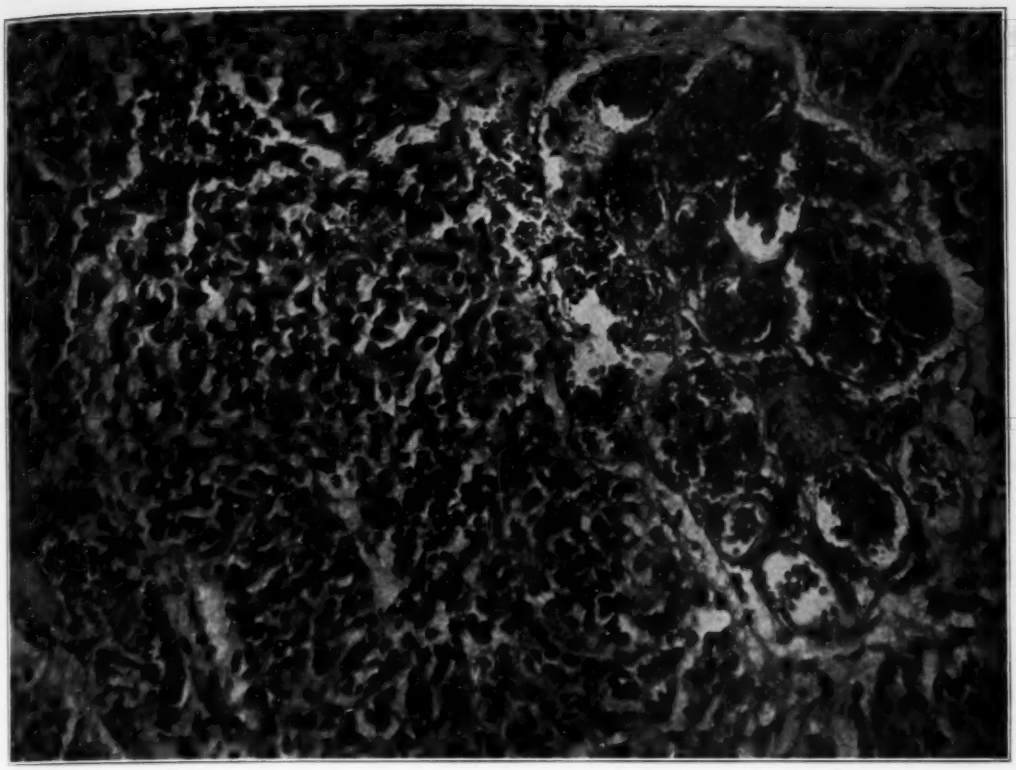

Fig. 11.—Section of pineal body of an infant, aged 13 months. The small dark cells are still fewer in number, but can be recognized as distinct from the large cells. Hematoxylin-eosin; reduced from a magnification of × 230.

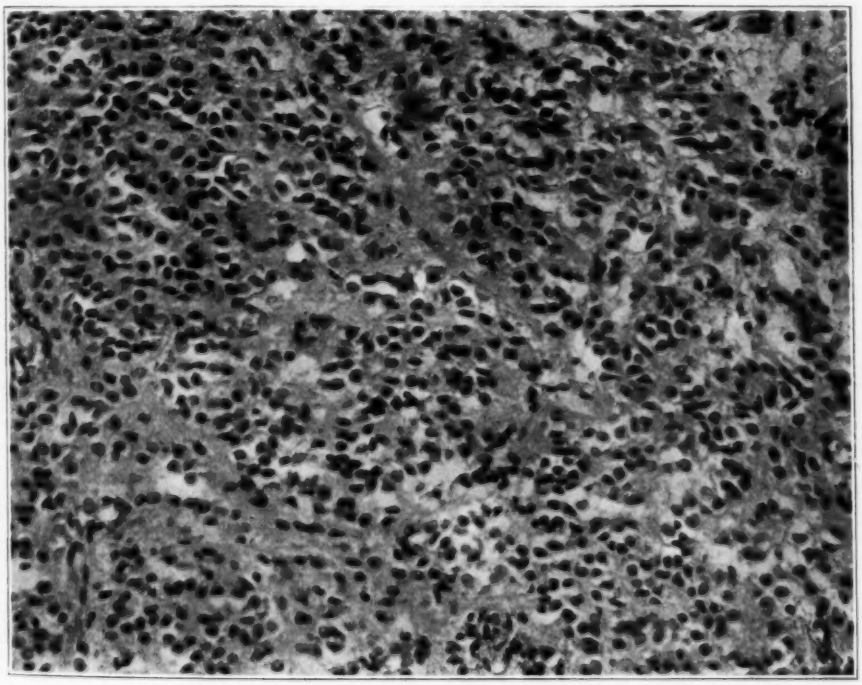

Fig. 12.—Section of pineal body of an infant, aged 18 months, showing the alveolar arrangement characteristic of this stage of development. Hematoxylin-eosin; × 230.

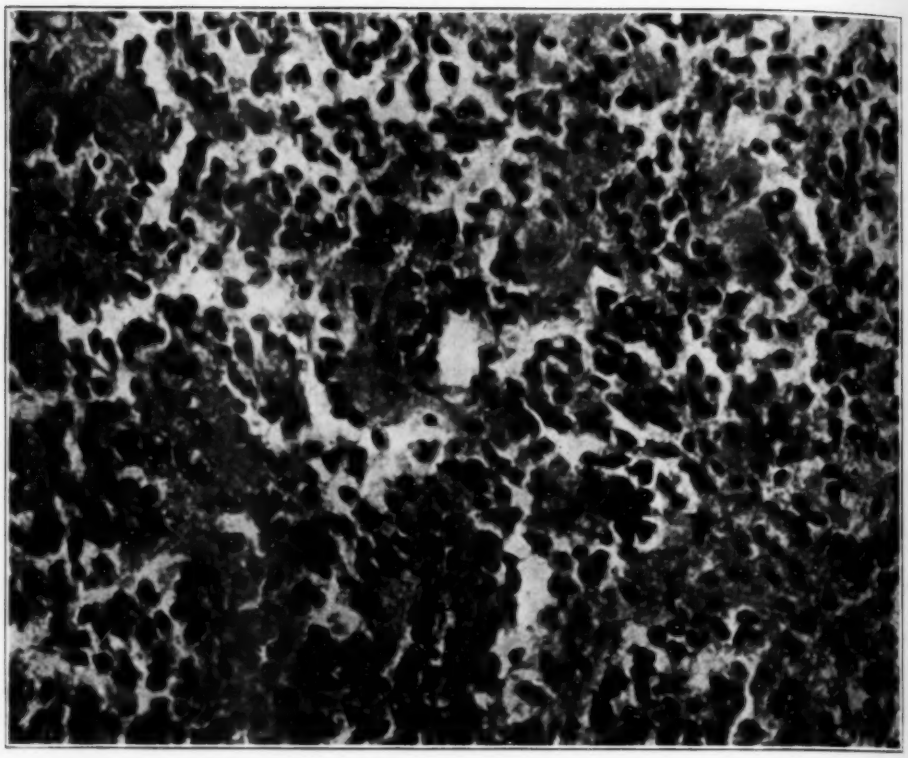

Fig. 13.—Section of pineal gland of an infant, aged 23 months.

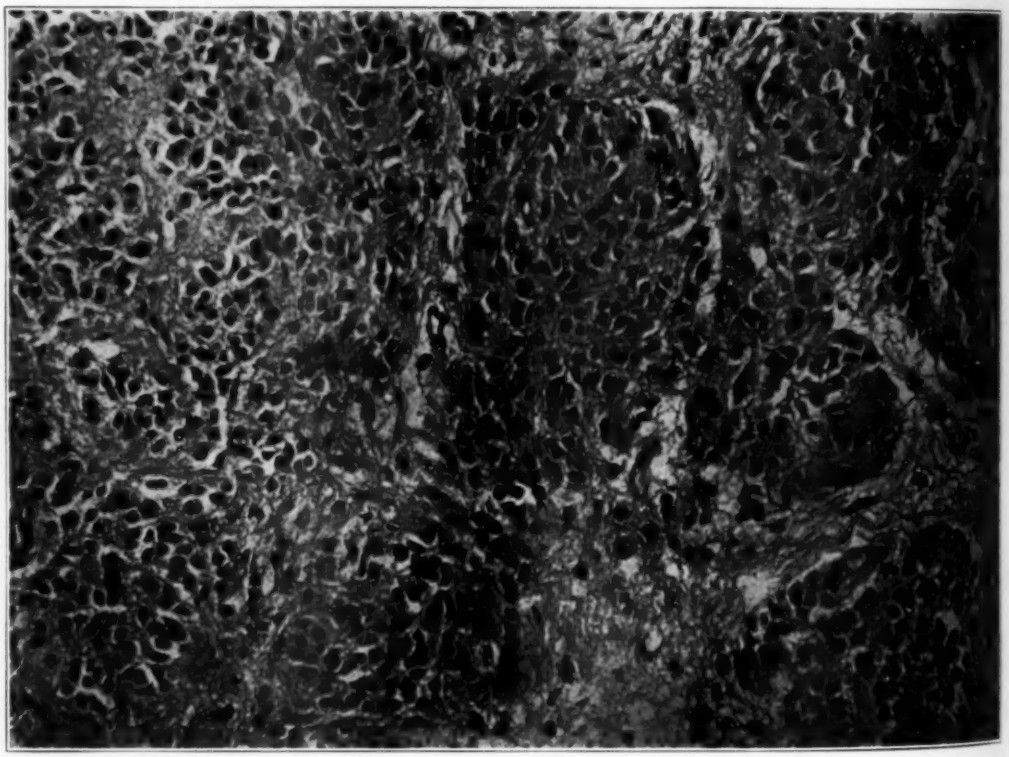

Fig. 14.—Section of pineal body of a child, aged 5½ years. Hematoxylin-eosin; reduced from a magnification of × 250.

At the end of 13 months the pattern so characteristic of the early days of postnatal life is hardly recognizable. Only an occasional accumulation of small cells is found in isolated areas (fig. 11).

At the end of 18 months the architecture that forms the transition between the infant and the adult form appears. Here one sees the alveolar arrangement of cells and the appearance of connective tissue

Fig. 15.—Section of pineal body of a man, aged 42. Hematoxylin-eosin; × 270.

trabeculae (fig. 12). This transition is still more apparent at 23 months (fig. 13), when a more definite alveolar pattern is assumed.

An additional feature noted in the pineal bodies of infants between the age of 18 and 23 months was the frequent occurrence of groups of basophilic granular cells, alongside of which there were also occasional large eosinophilic granular cells. This would seem to add weight to the belief that mesodermal components contribute their share in the organization of the pineal body.

From now on the architectural changes are not readily distinguishable over long periods. At 5½ years the structure of the pineal body approaches that of the mature gland. Isolated solid nests of cells are here surrounded by connective tissue (erroneously considered as glial) (fig. 14) and the general topography of the mature pineal gland is mapped out. The transition from now on until full maturity is so gradual that it is almost undetectable (fig. 15), and the late stages differ little in their basic histologic structure. The changes that occur now are mainly of a regressive character, with the formation of cysts, depositions of calcium, hyalinization and fibrosis.

REPORT OF CASES

CASE 1.—*Pincaloma in a boy. Structure of tumor uniform and characteristic of the early form of autochthonous growth in the pineal region. Clinical manifestations typical of a neoplasm in this location. No clinical evidence of pubertas praecox.*

History.—H. F., a boy, aged 13, had had the usual diseases of childhood, but otherwise was well up to 10 years of age. At that time he began to complain of headaches, which continued throughout the following three years. During the past year the headaches were associated with dizziness.

Examination.—The patient was underdeveloped. The pupils were unequal, the right being larger than the left, and did not react to light, but did react in accommodation. There was bilateral papilledema of 3 diopters. The deep reflexes were hyperactive and equal; the superficial reflexes were normal. Wassermann tests with blood and cerebrospinal fluid gave negative results.

Course.—In spite of the negative serology, but because of the Argyll Robertson pupils, the patient was regarded as suffering from juvenile dementia paralytica of tabetic type, and antisyphilitic treatment was given. The presence of papilledema, however, led to a strong suspicion of an intracranial neoplasm. The patient was allowed to go home, but was readmitted two months later complaining of intensified headache and vomiting.

Reexamination.—The pupils were fixed to light, but reacted normally in accommodation. There was bilateral external rectus weakness, more on the right than on the left. There was also a slight internal rectus weakness. There were generalized hyperreflexia with bilateral ankle clonus, a suggestive Babinski sign on the left side, slight ataxia in the right upper extremity, a cerebellar gait and posture with a tendency to fall to the right.

Subsequent Course.—At this time a neoplasm in the region of the quadrigeminal plate was diagnosed. To verify the diagnosis a ventriculography was performed and bilateral internal hydrocephalus was revealed. It was noted also that the posterior part of the third ventricle could not be detected, which indicated an extension of the tumor into this region. An exploratory craniotomy was performed, but it was not brought to completion because of active bleeding and a rapid decline in the condition of the patient. The patient died three weeks after the second admission.

Gross Anatomy.—The surface of the brain showed evidence of a marked increase in the intracranial pressure; the gyri were flattened, and the sulci were shallow. On accidental puncture of the cerebral hemisphere a large amount of clear cerebrospinal fluid escaped and the brain collapsed, assuming more normal

proportions. The tuber cinereum was markedly distended, stretching and thinning out the overlying optic chiasm. The cranial nerves at the base of the brain were partially lost on removal of the brain; those left intact, aside from a slight thinning, showed no apparent pathologic changes. When the cerebral hemispheres were separated and the corpus callosum, the quadrigeminal plate and the dorsal surface of the cerebellum were exposed, a large mass adherent to the falx cerebri was found protruding above the surface of the cerebellum for about 2 cm. It

Fig. 16 (case 1).—Tumor in the region of the quadrigeminal plate.

measured about 2.5 cm. in diameter. It infiltrated the quadrigeminal plate anteriorly (fig. 16) and the anterior border of the cerebellum posteriorly. This tumor mass, traced laterally, was found to infiltrate the cerebellum and the cerebral peduncle on the right side. On the left side it showed marked softening. The adjacent portion of the cerebellum was also softened and friable. The quadrigeminal plate was in front of the tumor and showed distinct subdivisions into the quadrigeminal bodies, the anterior being somewhat flattened and irregular in outline, the posterior narrowed, irregular and lacking the mesial fissure. The pineal body was not found.

Microscopic Anatomy.—This case was selected as the first of the group to be described because it illustrates the histologic architecture of a typical undifferentiated form of pinealoma. It was characterized by a striking mosaic, with streams of small, deeply staining cells enveloping nests of larger cells forming lighter areas. The second type of cells, because of their size, their vesicular nuclei and the larger masses of clear cytoplasm, formed a distinct cell type, bearing a strong resemblance to the parenchymal cells of the mature pineal body (fig. 17). The two types of cells, small and large, were segregated into separate areas, but occasionally a few of the small cells were dislodged into the clearer fields of the parenchymal cells.

Fig. 17 (case 1).—Section of tumor showing the characteristic mosaic arrangement of the two distinct cell types. Compare with figures 5, 6 and 7. Hematoxylin-eosin; reduced from a magnification of × 280.

A survey of the various histologic pictures presented by the pineal body in its postnatal evolution revealed that this architectural pattern was a close imitation of patterns seen in the pineal body of infants from 3 to 8 weeks of age (figs. 5, 6 and 7). There was a strong temptation to assume that the tumor, in its histologic make-up, recapitulated a chapter in the histogenesis of the pineal body. It added evidence in favor of the theory of an embryonal rest, particularly when applied to the formation of a tumor in the central nervous system. This was the dominating histologic picture in the larger part of the tumor mass, as shown by sections

prepared from numerous blocks taken from various parts of the tumor, but there were also areas that showed mild deviations from the typical cellular organization. In such fields the large cells remained unchanged in outline and in number, whereas the small cells showed a marked reduction in number, their place being taken by fibroblasts and collagenous fibers (fig. 18). It would seem that the collagenous fibers develop at the expense of the small round cells, as examination of many contiguous microscopic fields revealed that young fibroblasts develop among

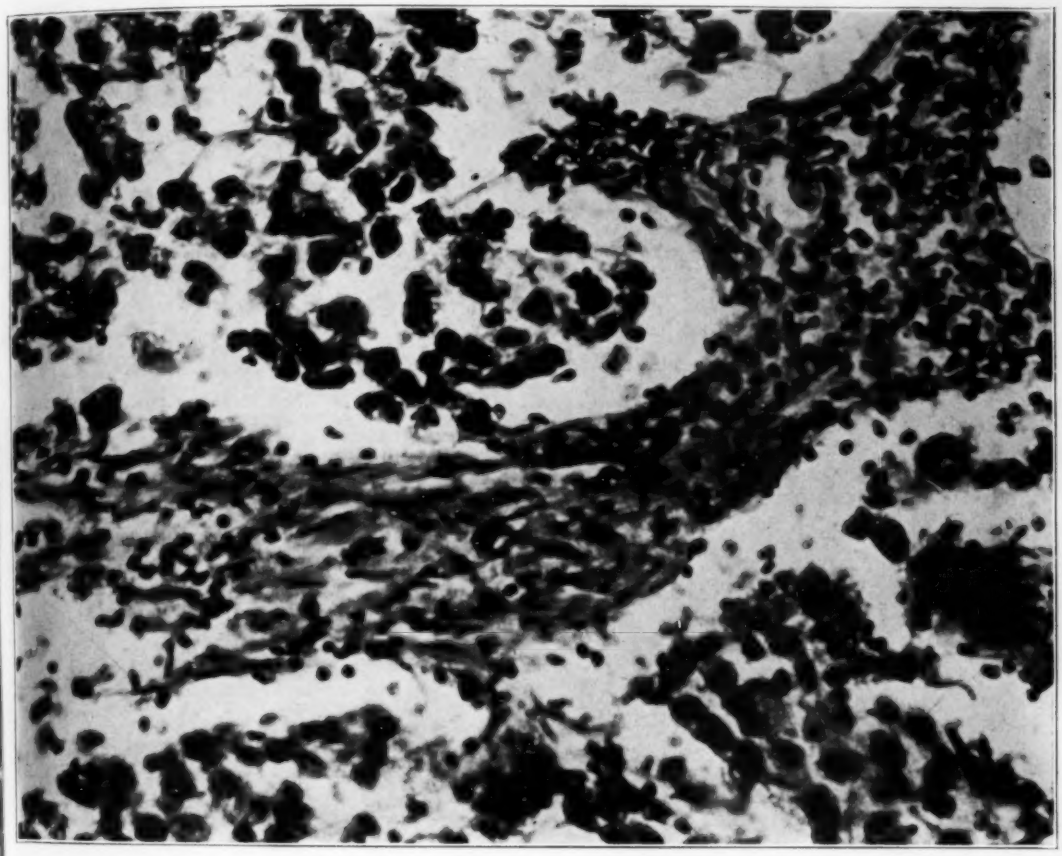

Fig. 18 (case 1).—Section of tumor showing formation of fibrous tissue, with simultaneous diminution of the number of small dark cells. Hematoxylin-eosin; × 370.

the gradually disappearing small cells (fig. 19). It is further emphasized by silver-stained preparations that where the small cells were in large numbers there was little fibrous structure, but as the small cells began to disappear a fine fibrillar structure came into view (fig. 20).

Giant cells (fig. 21) were not uncommon in various areas of the tumor. They were usually more numerous in the vicinity of calcified plaques, but were also found at some distance from such plaques. They commonly had the appearance

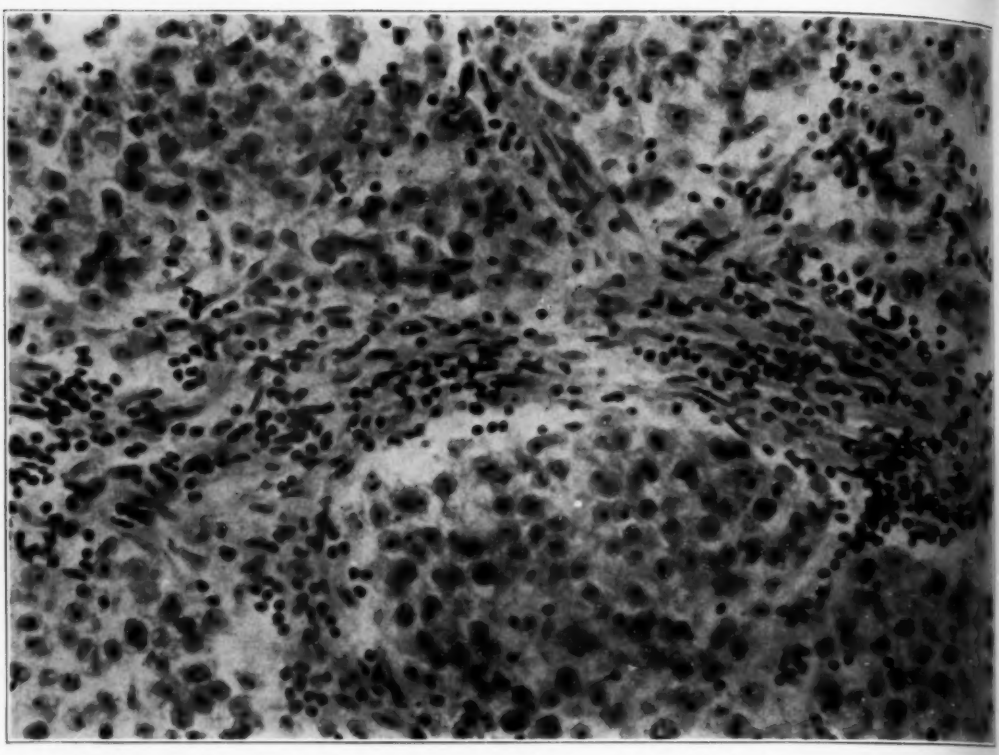

Fig. 19 (case 1).—Section of tumor showing the formation of fibroblasts. Hematoxylin-eosin; reduced from a magnification of × 350.

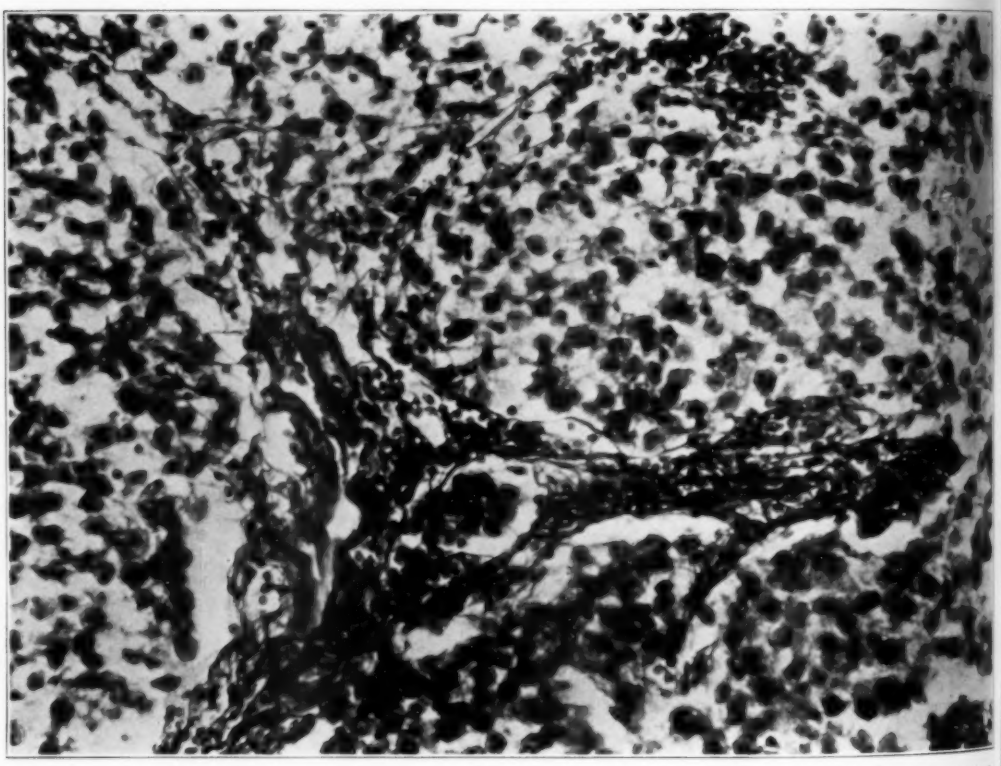

Fig. 20 (case 1).—Section of tumor showing fine fibers running through the masses of small dark cells. Globus modification of Hortega silver-carbonate stain; reduced from a magnification of × 350.

of foreign-body giant cells; but occasionally they had the character of large multinucleated macrophages with enclosures. The giant cells often assumed forms that have led some observers to the erroneous conclusion that they were ganglion cells. In our material no ganglion cells were found, although it is not improbable that such cells may occur when the tumor invades the brain stem. In such instances some cells properly belonging to the brain stem may become incorporated in the tumor, but are not really part of the neoplastic process.

CASE 2.—*Pinealoma in a boy. Structure of tumor fairly uniform and characteristic of the early form of an autochthonous growth in the pineal region. Strikingly similar to case 1. Signs and symptoms typical of a lesion in the pineal region. Also manifestations of vegetative dysfunction.*

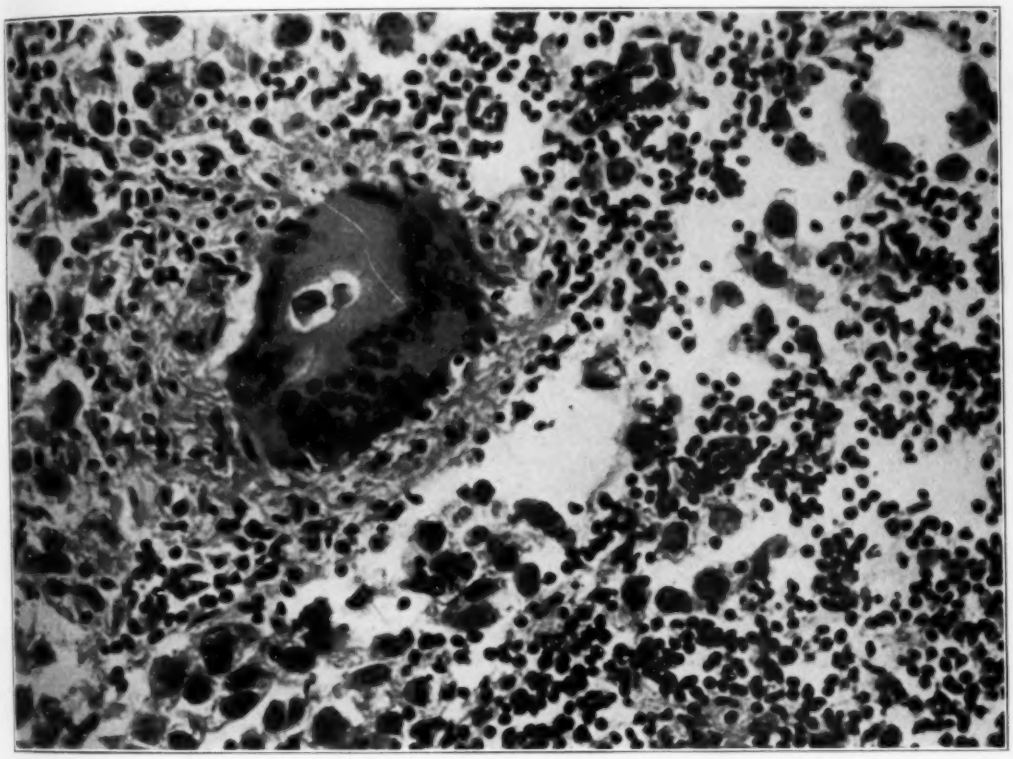

Fig. 21 (case 1).—Section showing irregularity in distribution of large and small cells, and a giant cell with enclosure. Hematoxylin-eosin; reduced from a magnification of × 375.

History.—S. A., a boy, aged 17, had had polydipsia and polyuria for about one year before admission to the hospital. His family and past histories were without significance. About four months before admission, there was a sudden change; headaches, vomiting spells and mental alterations developed; he had difficulty in concentration and became inefficient at school. More recently he had complained of double vision. He became disinterested and at times drowsy. It was noticed also that he dragged his right foot.

Examination.—The patient, who was rather unusually tall for his age, walked on a wide base and tended to stagger to the right. The chin was turned to the right and the occiput to the left. There were slight ataxia in the right hand and slight athetoid movements in the left hand. The deep reflexes were somewhat more active on the left side. There was bilateral papilledema, with hemorrhages and an elevation of about 4 diopters. The right pupil was larger than the left. The reaction to light was sluggish; the reaction in accommodation was not recorded. There were paresis of the right external rectus and limitation of upward gaze, which was more marked on the left. There was ptosis of the right eyelid. The Wassermann reaction of the blood was negative.

Course.—A tumor in the region of the third ventricle and aqueduct of Sylvius was suspected. Ventricular puncture with an injection of dye was performed. The ventricles were dilated, and the dye injected into one ventricle was easily recovered from the other, demonstrating that the foramina of Monro were open. Ventriculography showed a marked degree of internal hydrocephalus with the lateral and third ventricles greatly dilated. The posterior portion of the third ventricle was not seen and the roentgen diagnosis was: a lesion involving the aqueduct and posterior part of the third ventricle.

About two weeks after admission, an exploratory operation was performed. A large flap was made in the right occipital region. Owing to considerable bleeding, the operation was incomplete. Infection of the wound developed and a secondary operation had to be postponed on this account. Following this operation, the patient improved strikingly. He became alert and made no subjective complaint.

He was discharged three and a half months after admission and referred to the follow-up clinic. Here he was observed for four months. The paralysis of the right external rectus and the limitation of upward gaze continued to be present. The gait was unsteady. There was moderate ataxia in all four extremities. There were increased deep reflexes, and a Babinski sign on the left side, but the papilledema had disappeared and he was free from headache and subjective signs of increased intracranial tension. Up to six weeks before his second admission he had attended school, when what was described as pneumonia developed; since then he had declined rapidly, both mentally and physically.

Reexamination.—The patient was extremely emaciated. He showed marked mental deterioration. There were marked spasticity and contracture of the extremities with a bilateral Babinski sign. The pupils were irregular and unequal, the right being larger than the left.

Subsequent Course.—In view of the disappearance of the papilledema, the possibility of an inflammatory lesion was considered. Because of this, foreign-protein therapy was initiated. After the first injection the temperature rose slowly to 106 F. The patient's general condition declined, and death followed respiratory paralysis.

Gross Anatomy.—The brain was removed through the existing surgical wound. It was voluminous and under moderately increased pressure. When the occipital lobes were raised and the roof of the aqueduct of the fourth ventricle was exposed, a gelatinous semifluid mass was found covering those structures. The mass flowed freely. The character of the mass could not be established by gross examination. Though assumed to be neoplastic, its true character had to await histologic study. The pineal body was not found. The pituitary gland appeared normal. The tuber cinereum was very thin. The ventricles were much distended. The distention involved all divisions of the lateral ventricle and the third ventricle. The quadrigeminal plate was replaced by a large mass of soft, friable and granular

Fig. 22 (case 2).—Photograph showing location of tumor and the false channel in the tectum mesencephali.

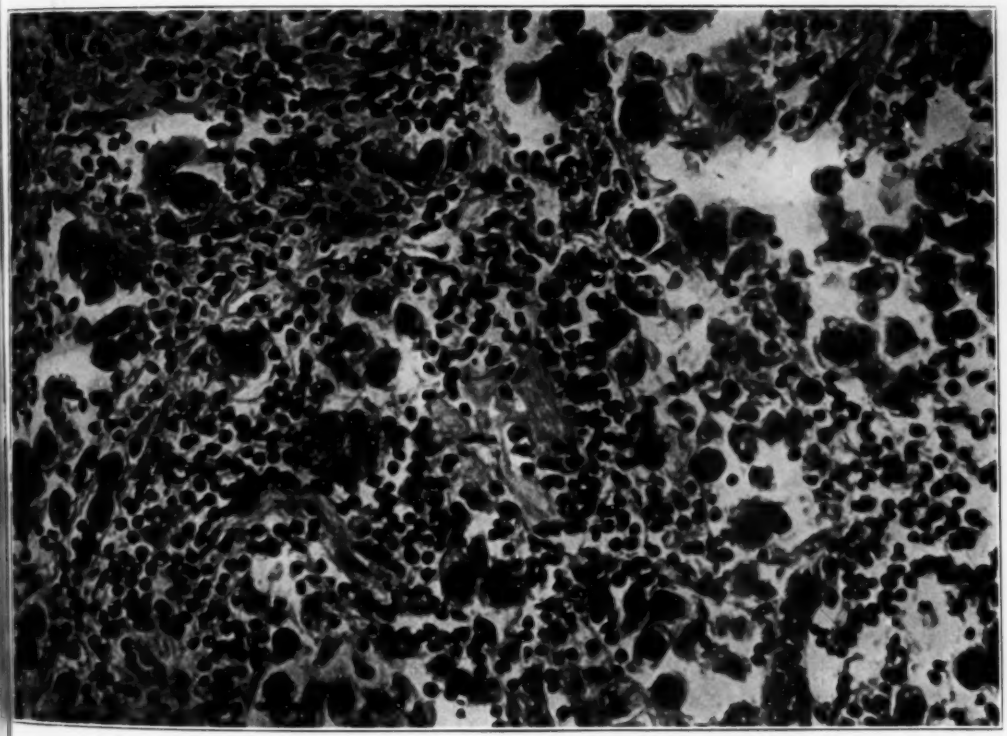

Fig. 23 (case 2).—Section of tumor illustrating its histologic appearance. The two cell types are less regular in arrangement than those in case 1. Hematoxylin-eosin; reduced from a magnification of × 360.

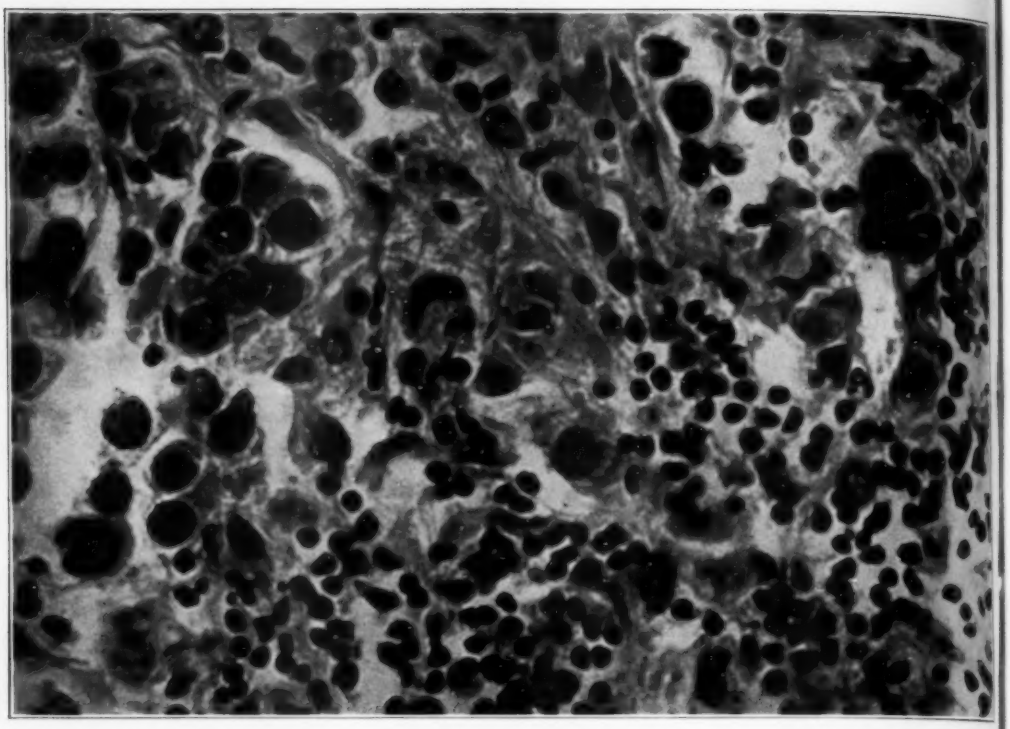

Fig. 24 (case 2).—Section of tumor under higher magnification, showing formation of fibroblasts. Hematoxylin-eosin; reduced from a magnification of × 480.

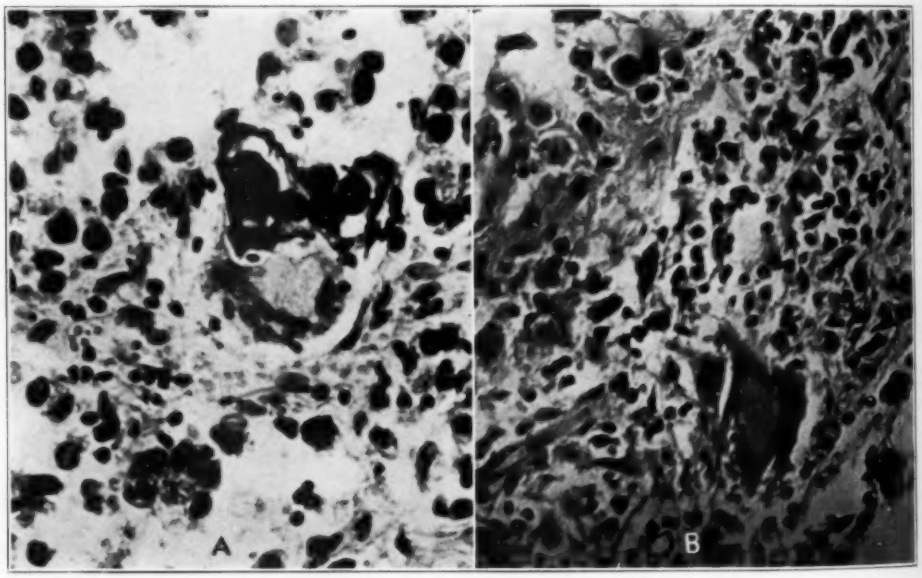

Fig. 25 (case 2).—Giant cells in tumor. Hematoxylin-eosin; *A*, × 375; *B*, × 280.

tissue (fig. 22). This mass measured about 2 cm. in width, 2 cm. in the anteroposterior diameter and about 3 cm. in depth posteriorly; a small calcareous body was found embedded in the depths of the mass. This was taken to be a remnant of the pineal body. The midbrain was markedly distorted, with its tectum and part of the tegmentum almost completely lost; the nucleus ruber was small, and the substantia nigra was poorly pigmented. The aqueduct was large and filled with a soft mucous matter. The fourth ventricle was of normal size and was filled with similar material.

Microscopic Anatomy.—The histologic composition of this tumor was almost identical with that of the previous one, and needs no detailed description. Here again, there was the beautiful mosaic, with the small cells forming streams that engulfed nests of the clear parenchymatous cells (fig. 23). The only difference was the smaller number of the dark, deeply stained, round cells and the larger size of the lightly staining parenchymal cells. The transition of the small round cells into fibroblasts was also present, though less marked (fig. 24). Mitotic figures were frequently seen in the large parenchymal cells. Giant cells of the foreign body variety were also noted (fig. 25). They were most frequently seen in the neighborhood of deposits of calcium (fig. 25*B*).

Case 3.—*Pinealoma in a boy. Structure of tumor less typical than in cases 1 and 2, with mild deviations from the characteristic architecture displayed in them. An example of tumor with the histologic structure corresponding to a later stage in the histogenesis of the pineal body. Clinical picture typical. No pubertas praecox.*

History.—P. S., a boy, aged 13, entered the hospital with a history of headaches of two years' duration. They would occur in attacks and would last for periods of from four to five hours. There were periods of several months when he was entirely free from such attacks. Four weeks before admission to the hospital, the patient began to have vomiting spells; one week later, he complained of double vision.

Examination.—The patient was well developed and well nourished. There was some anomaly in the distribution of hair; he had very thick hair on the head but none in the axilla, and a few stray hairs on the pubes. The external genitalia were rather larger than normal for his age. The pupils did not react to light, but reacted well in accommodation. There were: a paresis of upward gaze, a slight right external rectus weakness, ptosis of the right eyelid and bilateral papilledema of 5 diopters on each side. The visual fields were normal, and vision was reported as unimpaired. There was some weakness of the right arm and the left leg and a questionable Babinski sign on the left side. The deep reflexes were normal. A roentgenogram of the skull revealed calcification of the pineal body. The Wassermann reaction of the blood was negative. The cerebrospinal fluid was clear, colorless and contained no excessive number of cells.

Course.—On the basis of the history and physical signs a diagnosis of tumor of the quadrigeminal plate was made. Ten days after admission, an exploratory craniotomy was performed by means of an osteoplastic flap over the right parietooccipital region. Owing to a considerable loss of blood, only the first stage operation was carried out at this time. Ten days later, the second stage was performed. The occipital lobe was retracted, but no tumor was seen. A ventricular puncture revealed marked dilatation of the ventricles. Following the operation, complete paralysis of upward gaze developed, and the patient became increasingly lethargic. There was no recession in the papilledema. The condition declined gradually, and the patient was reduced to a vegetative state. He died six months later.

Gross Anatomy.—The brain showed evidence of increased intracranial tension. The right cerebral hemisphere was large and bulged in the right parieto-occipital region. On horizontal section, the ventricles were found greatly dilated, the right ventricular system somewhat more than the left. The third ventricle was likewise dilated. The pineal body was large, prominent and embedded in the tumor. It was calcified and attached to the firm tumor mass that occupied the region of the anterior notch of the cerebellum, resting on the quadrigeminal plate

Fig 26 (case 3).—Photograph showing location of tumor which is invading the pulvinar on the left side.

(fig. 26). The tumor was firm and grayish and appeared to invade the pulvinar on the left side. It measured about 2.5 cm. in diameter.

Microscopic Anatomy.—In this case, the histologic picture showed a definite departure from the microscopic structure of the two preceding cases. In spite of this, however, careful scrutiny of the material disclosed areas in which remnants

of the phase noted in the previous cases were discovered (fig. 27). On the whole, this tumor displayed a histologic structure indicative of an older, more differentiated phase in the development of the pineal body. Here, the small round cells had almost completely disappeared (fig. 28). A few of the cells could be seen at the periphery of the nests of parenchymatous cells. Their place for the most part was taken by robust bundles of collagenous fibers. In some areas, groups of small cells embedded in fibrous stroma dominated the field, while in other areas, connective tissue bundles with a few giant cells made the recognition of the real character of the tumor almost impossible (fig. 29). The giant cells in this instance

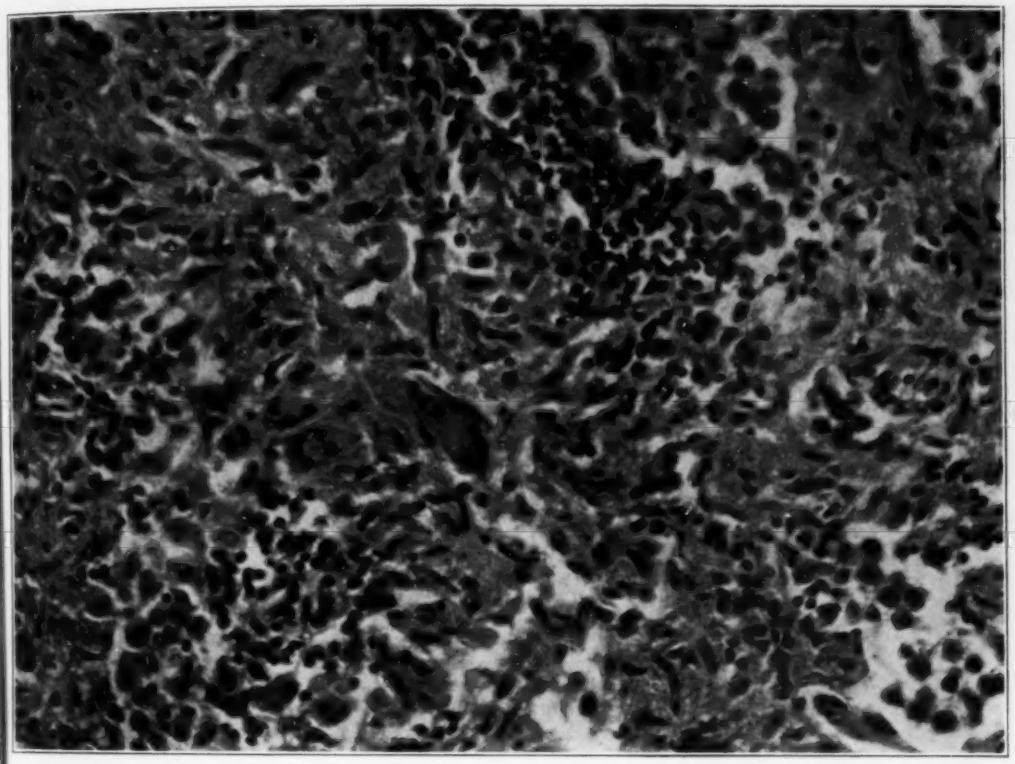

Fig. 27 (case 3).—Section of tumor showing the two cell types, though without the characteristic mosaic arrangement. A giant cell is seen surrounded by thick collagenous fibers. Hematoxylin-eosin; reduced from a magnification of × 290.

were foreign-body giant cells, and their staining properties were certainly not those of nerve elements. The finer structure of the collagenous fibers enclosing parenchymal cells is well demonstrated in figure 30.

CASE 4.—*Pinealoma in a man. A well encapsulated tumor, revealing in a few restricted areas the typical pattern of a pinealoma. Structures showing older histogenetic phases were more numerous. The pineal body was intact. Clinical picture typical. No pubertas praecox.*

History.—J. B., a man, aged 30, had been apparently well until nine weeks prior to admission to the hospital, when he began to suffer with headaches in the occipital region. At first these were mild and intermittent; later they became severe and continuous. At about the same time he began also to have projectile vomiting. He complained of generalized weakness, particularly in the lower extremities. There were no convulsions, but he became subject to fainting spells and somewhat later developed tremor on voluntary movement and some difficulty in speech, which gradually became more apparent. Two weeks before admission,

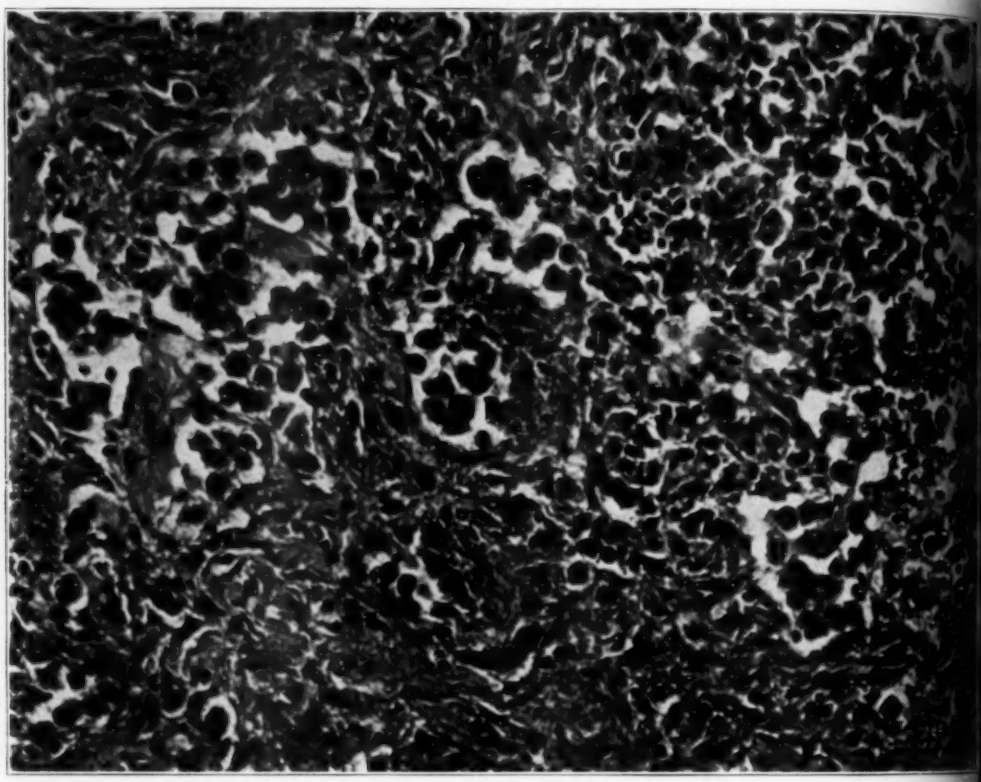

Fig. 28 (case 3).—Section from another part of the tumor. Nests of large cells are surrounded by massive bundles of connective tissue. In another part of the field the small cells are also seen. Hematoxylin-eosin; reduced from a magnification of × 400.

he began to have incontinence of urine. During the last week he experienced double vision.

Examination.—The patient was well developed and well nourished. He was irritable and confused. The head was in the cerebellar posture, with the chin to the left and the occiput to the right. The gait was cerebellar, with a tendency to fall backward and to the left. The pupils were unequal, the left being larger than the right; both reacted sluggishly to light; the reaction to accommodation was

not recorded. There was bilateral papilledema, with hemorrhages, and the elevation was 3 diopters on both sides. There was complete paralysis of the left external rectus and slight weakness of the right external rectus. There was ptosis of the right upper lid. No nystagmus was recorded. The reflexes on the right side were somewhat more active; there were no pathologic reflexes. Some ataxia was present in the left upper extremity. Caloric tests gave negative results.

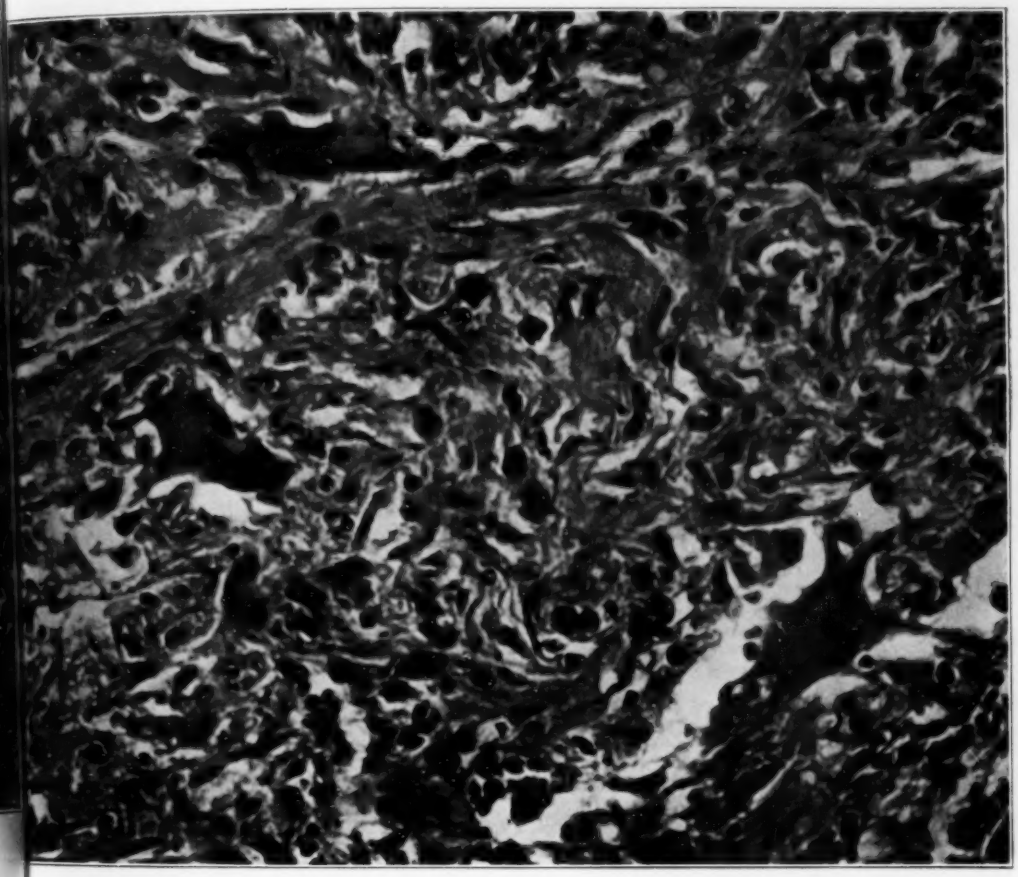

Fig. 29 (case 3).—Section of tumor showing a striking departure from the typical histology of a pinealoma. The large mass of collagenous fibers and the giant cells of the foreign-body type are not uncommon features of tumors of this type. Hematoxylin-eosin; × 420.

Course.—The history and physical signs were interpreted as indicating the presence of a neoplasm, probably in the posterior fossa. An exploratory craniotomy in two stages was performed. No neoplasm was found in the posterior fossa. Puncture of the lateral ventricles was performed. The ventricle on the right side could not be reached. The left ventricle was found markedly dilated, and more than 100 cc. of fluid was withdrawn. Following the operation, deviation of

the jaw to the left and definite involvement of the sensory fibers of the left branch of the fifth nerve were noted. The upward and downward gaze was normal. The papilledema did not recede. The patient became progressively more drowsy and died two months after admission.

Gross Anatomy.—The brain was under markedly increased tension. It was voluminous. The posterior lobes of the cerebellar hemispheres were adherent to the surgical wound and on removal of the brain were found to be much distorted. On the dorsal surface of the cerebellum in the region of the vermis there was a large mass (fig. 31), which extended laterally to both cerebellar hemispheres and

Fig. 30 (case 3).—Section showing the fibrous groundwork illustrated in figure 29. Globus modification of Hortega silver-carbonate stain; reduced from a magnification of × 450.

forward as far as the quadrigeminal plate. It measured about 7 cm. in its long axis, 6 cm. in the transverse diameter and about 8 cm. in the dorsoventral axis. The mass was encapsulated and separated easily from adjacent cerebellar tissue. It was irregular in outline, with several small nodules mounted on its dorsal surface. It was mainly subtentorial, being limited in front by the edge of the tentorium. It was separated from the fourth ventricle by a thinned out vermis. The vermis itself was not invaded by the tumor mass, but was depressed and flattened. The lateral ventricles were markedly enlarged, presenting a picture of

Fig. 31 (case 4).—Photograph showing location of tumor.

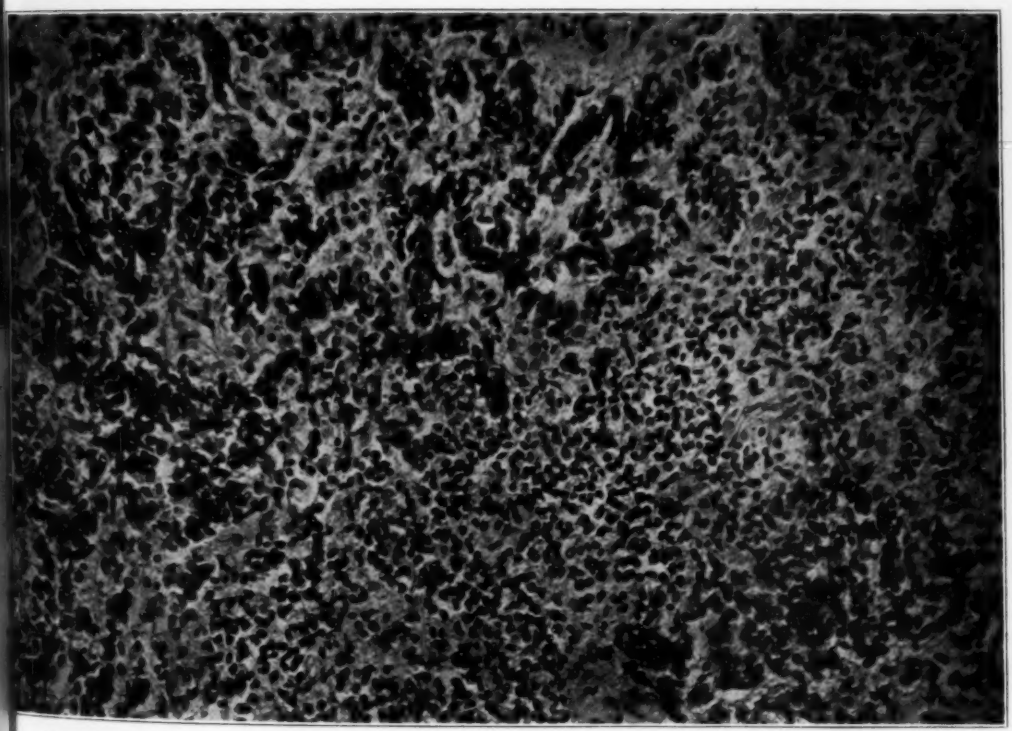

Fig. 32 (case 4).—Section of the tumor showing the two cell types but with less regularity in arrangement. Compare with figure 11. Hematoxylin-eosin; reduced from a magnification of × 250.

bilateral symmetrical internal hydrocephalus. The pineal body was found in its normal location and was normal in outline and size.

Microscopic Anatomy.—In this case, the structure of the tumor showed a still greater departure from the typical architectural patterns of tumors of this type, and also showed a greater variability in structural design. Still it was possible to demonstrate the basic morphologic feature shown in the preceding three cases. Somewhat wider streams of the small, dark cells were found, splitting larger aggregations of the "parenchymal" cells (fig. 32). The latter now approached in character the parenchymal cell of the mature pineal body. The organization of the cellular elements was of a type found in an older phase in the development

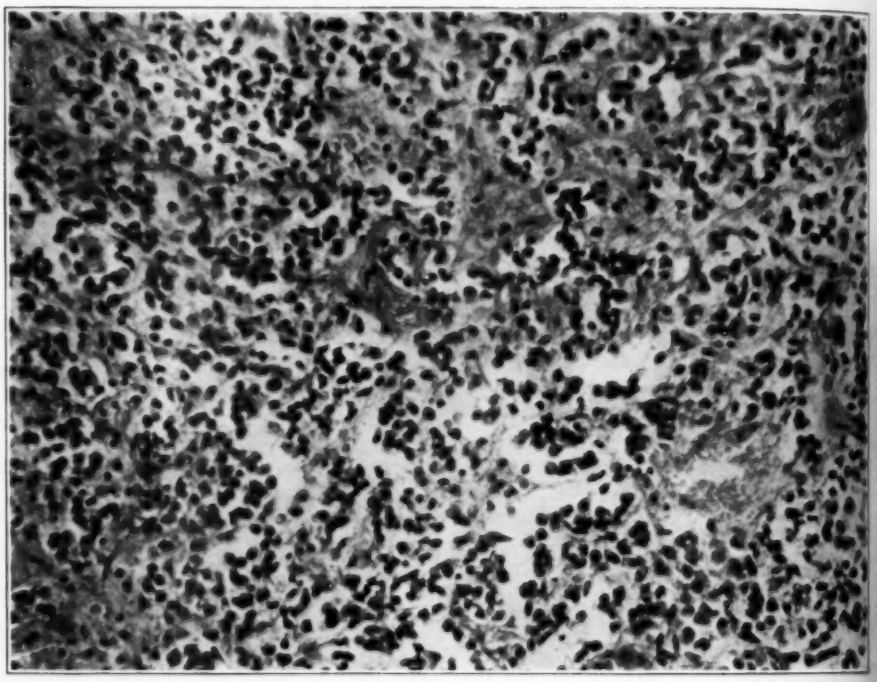

Fig. 33 (case 4).—Section taken from another part of the same tumor as in figure 32, showing arrangement of alveolar cells. Compare with figures 12 and 13. Hematoxylin-eosin; × 240.

of the organ (fig. 11). In other parts of the tumor cellular organizations were seen that resembled more histogenetic phases (fig. 33; compare with figs. 13 and 14).

CASE 5.—*Pinealoma in a man. An encapsulated tumor in an unusual location, to the left of the midbrain. Histologically, a variety of cellular arrangements, each corresponding to some stage in the development of the pineal body. Clinical picture typical. No pubertas praecox.*

History.—O. O., a man, aged 37, had been well up to the age of 35. At that time he began to have some difficulty with vision and for a time saw double. He also had occasional headaches. These symptoms continued with increasing severity up to the time of his first admission to the hospital.

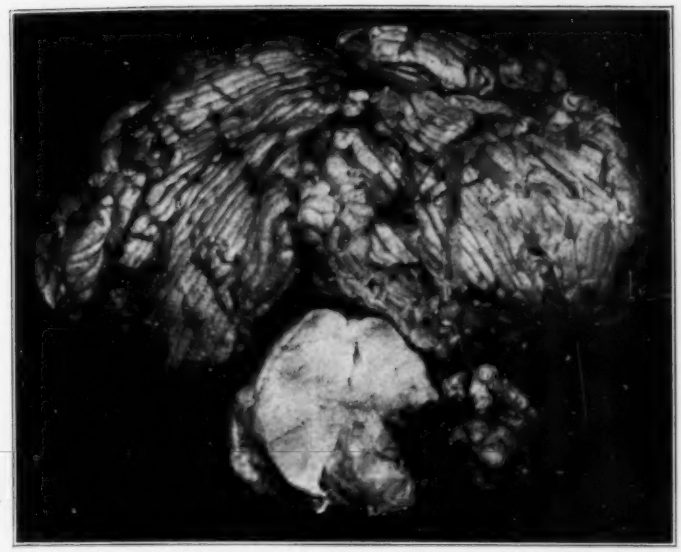

Fig. 34 (case 5).—Photograph showing the unusual lateral location of the tumor.

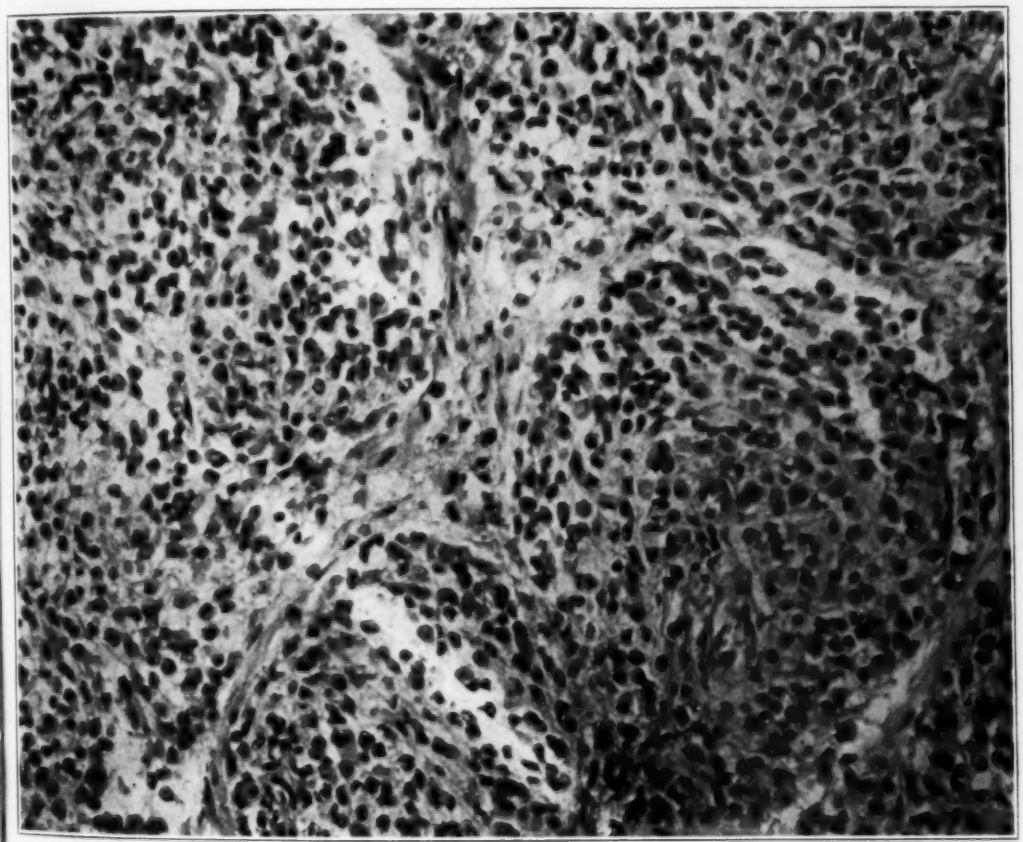

Fig. 35 (case 5).—Section of tumor; the true character of its histology is recognized by comparing it with the structure of the pineal body in early childhood (fig. 14). Hematoxylin-eosin; × 210.

Examination.—The patient was normally developed; the pupils were dilated and responded sluggishly to light but normally in accommodation. There was a distinct impairment of the upward gaze. The fundi were hyperemic, but were otherwise normal. The visual fields were normal. There were slight bilateral internal rectus weakness and slight facial weakness. The deep reflexes were more active on the right side. The superficial reflexes were normal.

Course.—The patient was thought to be suffering from a neoplasm of the midbrain. To verify this diagnosis a ventricular estimation was performed. Both

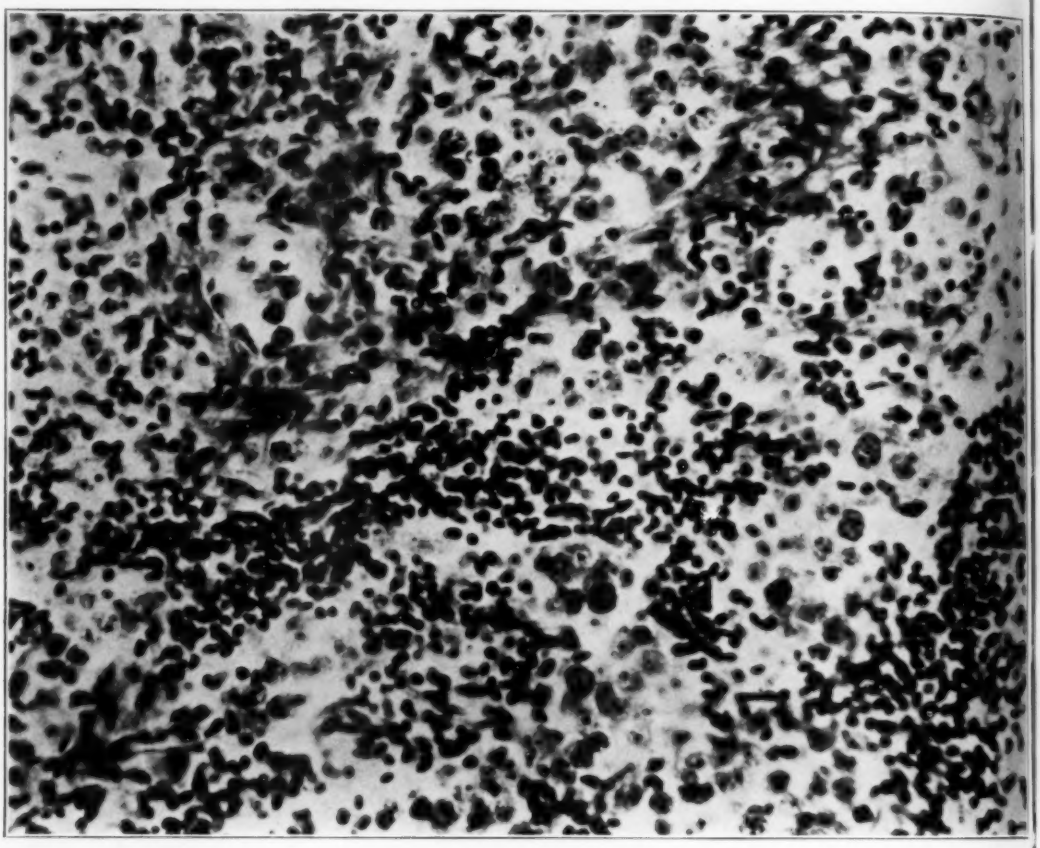

Fig. 36 (case 5).—Section taken from another part of the same tumor as in figure 35, in which the characteristic features of a pinealoma are readily recognized. Hematoxylin-eosin; × 350.

ventricles were punctured and found markedly dilated. Phenolphthalein injected into one ventricle promptly appeared on aspiration of the other. The conclusion drawn from this was that there was a bilateral hydrocephalus and that the foramina of Monro were patent. The patient remained in the hospital for three weeks, during which he had a normal temperature but a slow pulse. He complained of moderate headache, which was relieved by mild sedatives. During the

latter part of his stay in the hospital, he had several convulsive attacks characterized by stiffening of the left and at times of the right side of the body, without loss of consciousness. At the end of three weeks, he was allowed to return home. He remained at home for another three weeks, and on his return to the hospital all of the symptoms had become intensified. He now complained of daily headaches and blurring of vision. There were definite failure of memory and impaired mentality. There had been no further convulsions.

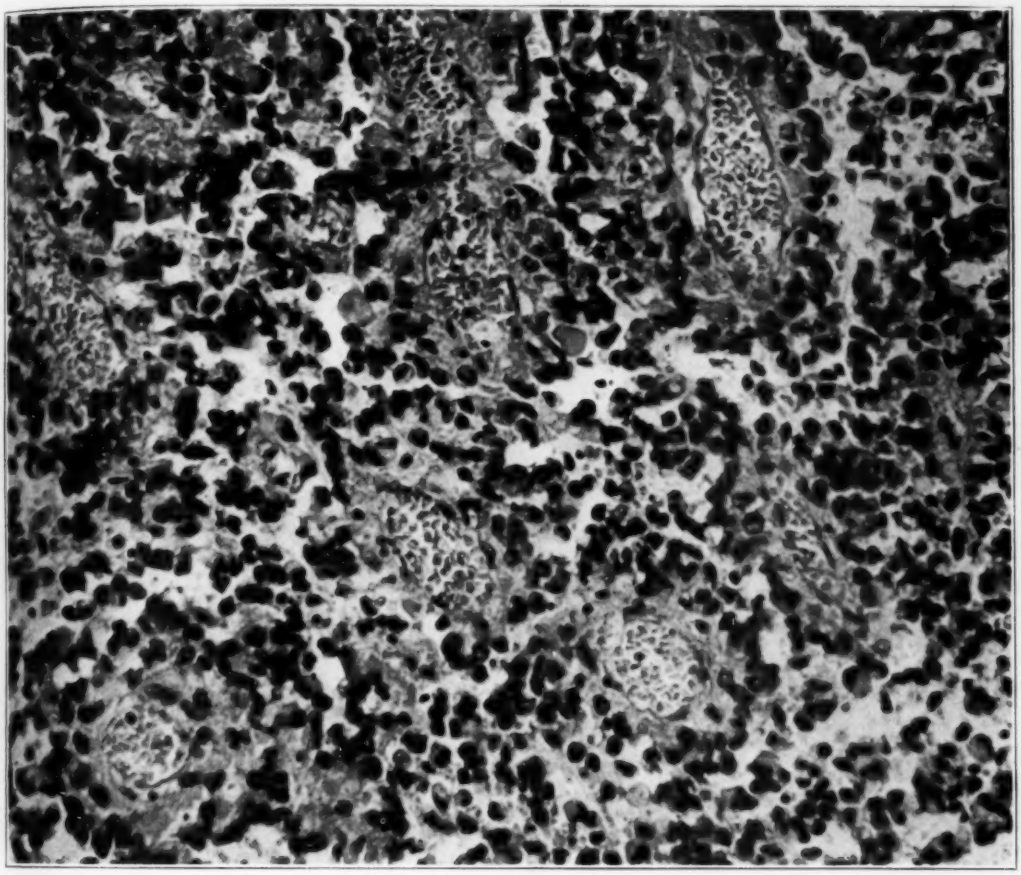

Fig. 37 (case 5).—Section from still another part of the tumor, showing another type of cellular arrangement. Compare with figure 13. Hematoxylin-eosin; × 260.

Reexamination.—The right pupil was much smaller than the left; both reacted sluggishly to light and normally in accommodation. There were limitation of upward gaze, weakness of the right external rectus muscle, slight right facial weakness, hyperactive but equal deep reflexes, active superficial reflexes and a Babinski sign on the right side. There were no sensory changes and no cerebellar phenomena. The fundi showed moderate blurring, but no measurable elevation.

Subsequent Course.—One week after admission, a suboccipital craniotomy was performed. Owing to the great amount of bleeding, only the first stage was completed. Two weeks later, the second stage was carried out. The posterior fossa was carefully explored, and no evidence of new growth was found. Following the second stage operation, an infection of the wound and signs of meningitis developed. The patient died a month after the second admission.

Gross Anatomy.—A limited examination through a suboccipital operative field revealed a tumor on the dorsolateral aspect over the quadrigeminal plate (fig. 34). The tumor was well encapsulated and easily separable from the substance of the adjacent midbrain. It measured about 5 cm. in the greatest diameter. It was irregularly round and nodular. Because of the limited opening through which the tumor was removed, no thorough search for the pineal body itself could be made; hence it is not definitely known whether the pineal body was intact.

Microscopic Anatomy.—From the first impression gained on routine examination of histologic material in this case one might be led to make an incorrect diagnosis. The solid groups of polygonal cells, surrounded by wide zones of connective tissue stroma (fig. 35), recalled the architecture of an endothelioma. The location of the tumor and its pedunculated attachment to the periphery of the midbrain made such a diagnosis plausible. However, guided by experience with other pineal new growths, further search was prompted and sections were made from other parts of the tumor and different pictures were obtained. Among them were apparent the characteristic mosaic, with alterations between the small deeply stained and the large clear cells (fig. 36), and other architectural patterns. When correlated with the various stages in the development of the pineal gland, these differing histologic pictures were found to be expressions of different developmental phases, each indicating an embryonal milestone. Thus, in figure 37, the cellular organization, which might easily be regarded as perithelioma, finds its analogy in the developmental stage illustrated in figure 13.

CASE 6.—*Pinealoma in a young child. The tumor invaded the quadrigeminal plate and adjacent structures. The pineal body was well preserved. The tumor revealed a histologic picture corresponding to several phases in the evolution of the pineal body. No apparent pubertas praecox.*

History.—M. S., a boy, aged 20 months, who was born at term, developed apparently normally until the onset of the present illness. Five weeks before admission to the hospital, the child fell backward, striking his head. There were no apparent symptoms until three hours later, when he bled from the mouth for ten minutes. During the next two weeks he vomited frequently, and then passed through a convulsive episode, lasting about ten minutes, in which the whole body became rigid. He was taken to a hospital, where he remained for two weeks. No definite diagnosis was made there, and he was taken home. He continued to vomit repeatedly and became apathetic and listless. In the forenoon, on the day of admission, he had another generalized spasm, lasting about ten minutes, and then he passed into a condition of decerebrate rigidity and lost consciousness. He was then taken to Mount Sinai Hospital.

Examination.—The child was in a coma, in a state of decerebrate rigidity, with the body rigid and all extremities in extension. The knee jerks and the abdominal reflexes were absent. The fundi showed a moderate papilledema. A lumbar puncture yielded clear fluid under markedly increased pressure, containing 60 lymphocytes. The patient died shortly after admission.

Gross Anatomy.—The convolutions of the brain were flattened, and the gyri were shallow. There was marked internal hydrocephalus. When the occipital

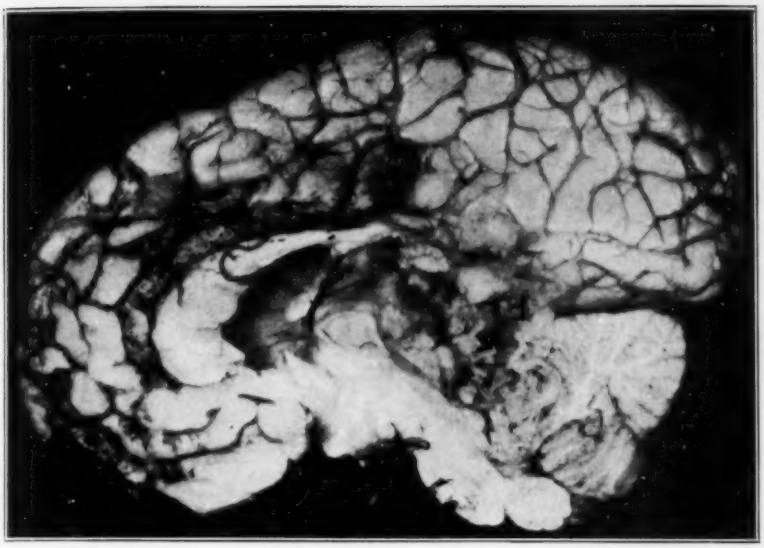

Fig. 38 (case 6).—Photograph showing size, location and invasive character of the tumor.

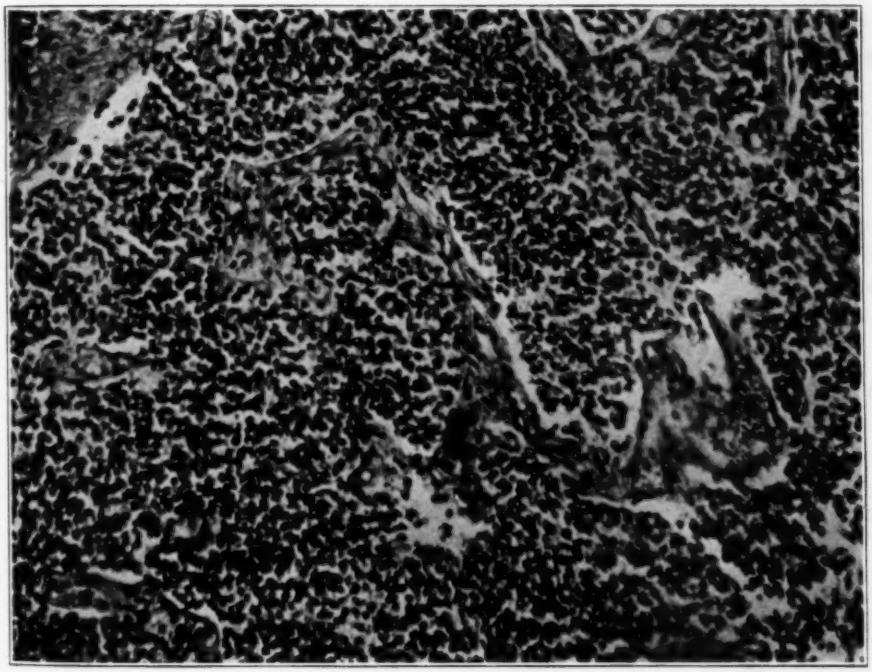

Fig. 39 (case 6).—Section of an apparently normal pineal gland. Hematoxylin-eosin; × 210.

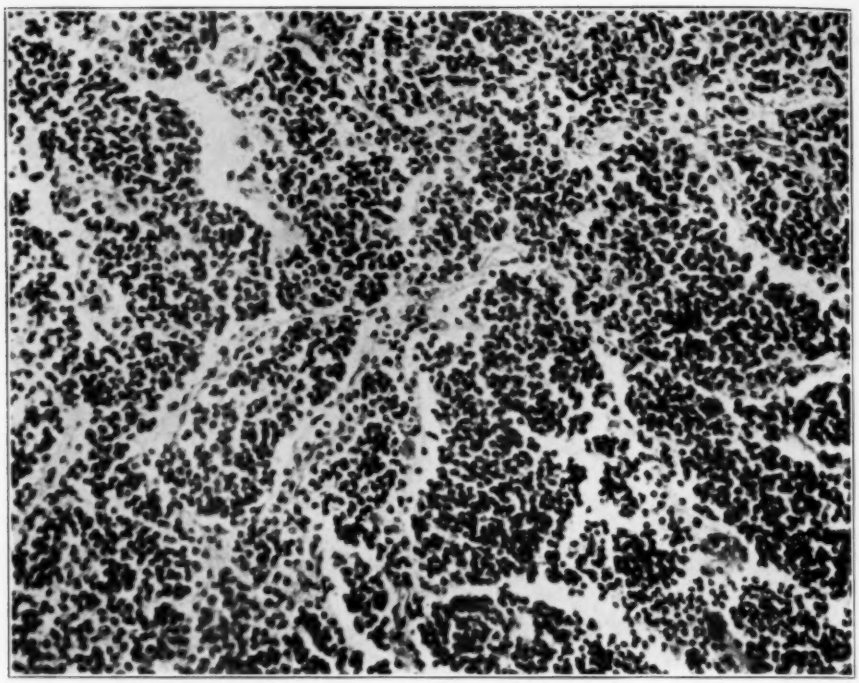

Fig. 40 (case 6).—Section of tumor, showing striking similarity in structure to the pineal gland (fig. 39). Hematoxylin-eosin; × 210.

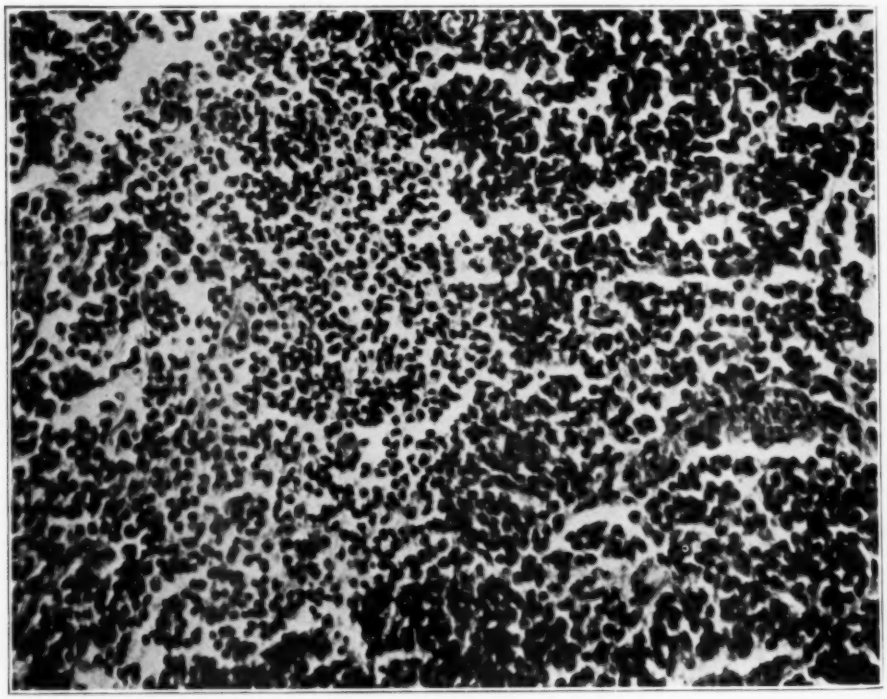

Fig. 41 (case 6).—Section of tumor showing the two characteristic cell types. Hematoxylin-eosin; × 210.

lobes were raised, a soft necrotizing tumor mass was exposed. It extended forward to the pineal region and posteriorly invaded the vermis of the cerebellum. The pineal body was found in its normal location.

When the brain was sectioned in a median sagittal plane, the tumor was found over the quadrigeminal plate (fig. 38), extending backward and invading the anterior portion of the vermis of the cerebellum. The tumor had a varied appearance. At its anterior extremity it was granular, soft and necrotic. In its most dorsal portion and somewhat posteriorly it was represented by a large nodule of hard granular material. More ventrally and posteriorly, where it invaded the cerebellum, it was smooth. Another nodule was found invading the median surface of the right occipital lobe in the region of the common stem of the parieto-occipital and calcarine fissures.

Microscopic Anatomy.—This case presented no difficult problem in the identification of the character of the tumor. It revealed, however, some interesting appearances. A comparison of figures 39 and 40 will immediately show the striking similarity between the structure of the pineal body in this case and the cellular make-up of the tumor. The lobulation, the formation of fairly solid cords, or irregularly round masses of cells, and the connective tissue trabeculae were present in both the pineal body and the tumor, but they were more marked in the pineal gland. On further scrutiny of the material in search of other histologic pictures in the same tumor, we found only two mild departures in the direction of the less mature pineal structure.

Thus, in figure 40 we found the two distinct zones, one consisting of an irregular mass of the small, round, deeply staining cells, abutting against an area made up of the larger, little differentiated, parenchymal cells. The latter zone, when compared with figures 9 and 11, will show the close resemblance to the pineal structure normal for this stage of development.

The invasive character of these tumors was well shown where the cerebellar cortex was reduced to a narrow zone by the pressure exerted by the invading tumor, which was continuous with the main process of the tumor.

CASE 7.—*Pinealoma in a young girl. A large colloidal cyst with a small area of neoplastic tissue, completely displacing the tectum mesencephali and invading the right lateral ventricle. The structure of the tumor resembled that of a fully differentiated adult pineal body. Clinical picture of a posterior fossa neoplasm. No pubertas praecox.*

History.—A. G., a girl, aged 11, had been apparently well until two years before examination, when she fell down a flight of stairs and landed on her head. Her recent illness dated back to four months before admission, when she complained of abdominal pain, nausea and occasional vomiting. Her condition remained unchanged until two months before admission, when she began to complain of headache. For five weeks before admission, she had diplopia and difficulty in vision. She stated that she could see better on lateral gaze than on looking straight ahead.

Examination.—The patient was well nourished and appeared drowsy, but could easily be aroused. She was resistant to examination and irritable. The neurologic signs were meager. There was frequent yawning. The deep reflexes were depressd, with no inequality and no pathologic reflexes. The gait was unsteady, with a tendency to fall to the right. There was a cerebellar posture of the head, with the chin to the right and the occiput to the left. Bilateral papilledema, with an elevation of about 2 diopters, was noted. The pupils were equal and reacted

sluggishly to light; reaction in accommodation was not recorded. Ptosis of the right eyelid and weakness of conjugate deviation to the right were observed. There was no nystagmus. The secondary sexual characteristics were within normal limits. The cerebrospinal fluid was reported as normal, and the Wassermann reaction of the blood was negative.

Course.—A diagnosis of neoplasm near the aqueduct of Sylvius was made. A two-stage suboccipital craniotomy was performed, but no tumor was seen in the posterior fossa. The patient's vision declined rapidly, and she became totally blind, with the pupils fixed to light. She also became entirely deaf. Six weeks after admission, the right upper and lower extremities were completely paralyzed

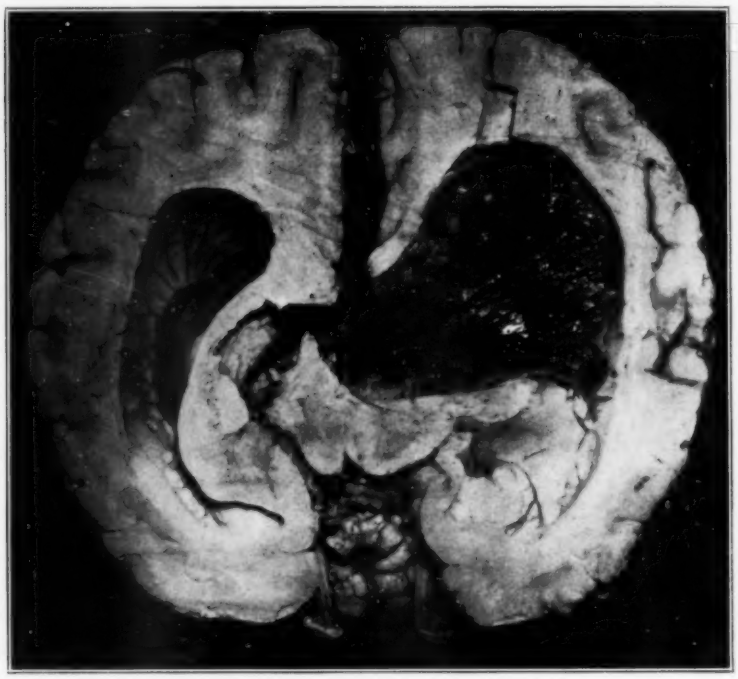

Fig. 42 (case 7).—Photograph showing location of tumor and its extension into the lateral ventricle.

and showed resistance to passive movement, but no contractures were present. The left upper and lower extremities were freely movable. There was a curious posture of the left hand; the wrist was flexed and the fingers were slightly extended, and there was a slow, rhythmic coarse tremor of the left hand. The patient deteriorated slowly, and died ten weeks after admission.

Gross Anatomy.—The brain showed evidence of increased intracranial tension. The posterior inferior part of the cerebellum was adherent to the surrounding meninges and its removal necessitated some tearing of the tissues. When the occipital lobes were lifted, a soft tumor was exposed. It extended from the superior vermis to the quadrigeminal plate and further forward, as was revealed when the brain was cut. A large colloid cyst was found occupying the right lateral ventricle (fig. 42). It completely filled this ventricle as far forward as

the foramen of Monro and posteriorly as far as the junction of the descending and posterior horns. It then extended backward over the roof of the aqueduct of Sylvius, where it embedded itself in a depression over the lateral lobe and vermis of the cerebellum. In its posterior extent it almost completely destroyed the tectum of the midbrain and some of the tegmentum on the left side. The ventricular cavities were markedly distended. The third ventricle was widely open, but was displaced to the left and deformed. The cyst had a well defined capsule which measured about 2 mm. in thickness. It was free in its anterolateral aspect but adherent to adjacent tissues in its ventral-median aspect. It was filled with

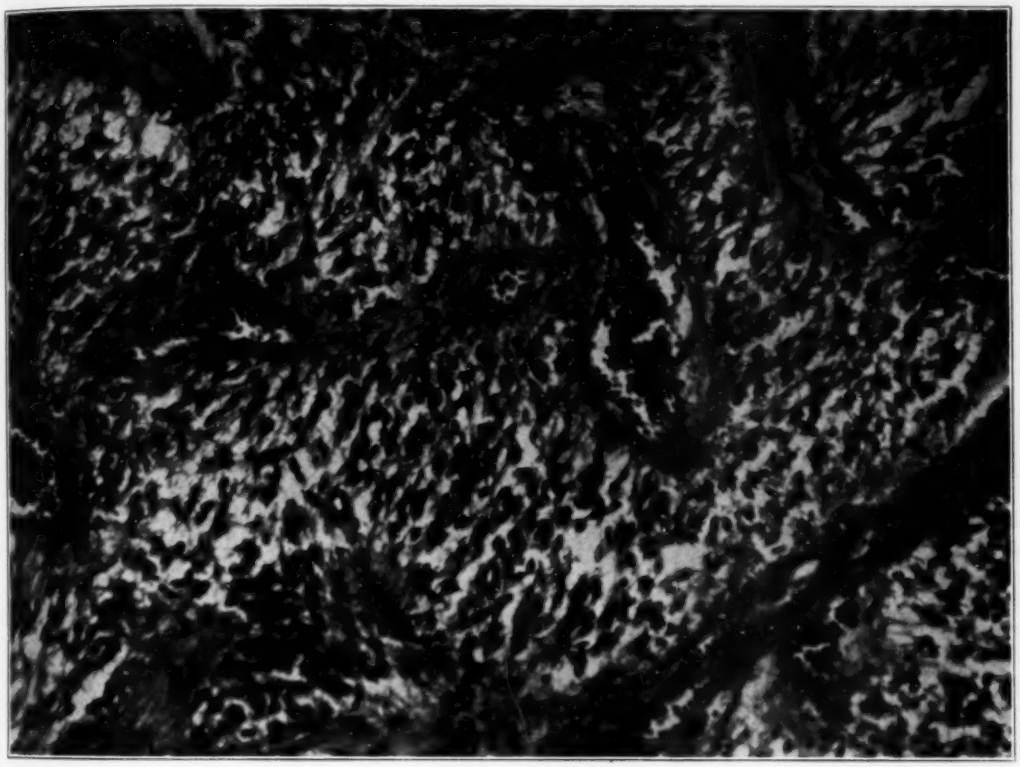

Fig. 43 (case 7).—Section of the tumor, showing the close resemblance to the structure of a normal mature pineal body. Compare with figure 15. Hematoxylin-eosin; reduced from a magnification of × 270.

jelly-like substance, was grayish green and on its ventral surface presented a small, spongy mass which in some parts was cystic. These areas bore a striking resemblance to the structure of the pineal body. The pineal body could not be found.

Microscopic Anatomy.—Little need be said about the finer structure of this tumor. A glance at figure 43 will immediately make apparent its main features. Its strong similarity to the adult pineal gland (fig. 15) would at first suggest a diagnosis of pineal hyperplasia. Such diagnoses are occasionally made. But it is

rather difficult to draw a distinct line of differentiation between hyperplasia and new growth. In this instance, because of the youth of the patient and the size of the tumor, the neoplastic character is the more likely. Here, however, the pinealoma is of the highly differentiated make-up that may be classed as an adult pinealoma.

COMMENT ON THE CLINICAL OBSERVATIONS

An analysis of the clinical data presented (accompanying table) reveals that six of the patients were male and one was female. Four of the seven were at, or younger than, puberty. In only one was any unusual genital development noted, and this was not striking. All of the patients presented the usual symptoms of tumor of the brain—headache, vomiting and vertigo—and, in addition, five of the seven gave a history of diplopia. The striking physical signs that aided in localization were related to the innervation of the muscles of the eyes. Argyll Robertson pupils (either complete or incomplete) were present in six cases, and in all of these were accompanied by paresis of muscles of the eyes. Thus it may be said that interference with conjugate movement of the eyes, particularly limitation of upward gaze, is the important localizing symptom in tumors in this region. Papilledema was present in all of the cases. It is noteworthy that four of the seven cases gave signs of cerebellar involvement, which were sufficiently prominent to cause some confusion in the clinical diagnosis. In one case the papilledema receded during the clinical course. This created some doubt as to the accuracy of the original diagnosis of tumor of the brain, and the probability of an inflammatory process was considered. The explanation for this rather unusual phenomenon was later found in the discovery of a new channel for the drainage of the cerebrospinal fluid, established as the result of destruction of tissue near the occluded aqueduct.

COMMENT ON THE ANATOMIC OBSERVATIONS

Macroscopic Data.—Six of the seven tumors herein described were found in the region of the quadrigeminal plate. One lay in an unusual location, on the side of the midbrain. The latter and one other of this group (cases 4 and 5) were well encapsulated and showed no invasive tendencies. The other five (cases 1, 2, 3, 6 and 7) invaded the tectum of the mesencephalon, the adjacent portion of the cerebellum, mainly the vermis, and extended forward into the region of the basal ganglia. In two instances (cases 2 and 6) the tumors invaded the cerebral hemisphere, and in one case (case 7), in which the tumor was largely cystic, it completely filled a lateral ventricle. Softening processes in the tegmentum of the midbrain and pons were present in four cases (cases 1, 2, 6 and 7). Bilateral symmetrical hydrocephalus was found in every instance and was due to compression of the aqueduct by the

Clinical Data in the Seven Cases Presented

Case	Age and Sex	Length of Clinical Course	General Symptoms	Visual Disturbances	Ocular Palsies and Changes in the Disk	Sexual Precocity	Vegetative Dysfunction	Cerebellar and Extrapyramidal Tract Signs	Pyramidal Tract Signs
1	13 yr. ♂	3 yr.	Headache; dizziness; vomiting	None	Argyll Robertson pupils (inc.); limitation of upward gaze; right external rectus weakness; bilateral internal rectus weakness; papilledema	None	None noted	Ataxia of right upper extremities; cerebellar posture and gait	Slight right facial; bilateral hyperreflexia; bilateral ankle clonus; left Babinski sign
2	17 yr. ♂	1½ yr.	Headache; vomiting; impaired mentality; drowsiness	Diplopia	Argyll Robertson pupils (inc.); paresis of upward gaze; weakness of right external rectus; ptosis on right; papilledema	None	Polyuria and polydipsia	Cerebellar posture and gait; adiadokokinesis of left hand	Increased deep reflexes on left; Babinski sign on left
3	13 yr. ♂	2½ yr.	Headache; vomiting	Diplopia	Argyll Robertson pupils; paralysis of upward gaze; weakness of right external rectus; ptosis on right side; papilledema	Genitalia larger than normal	None noted	None	Slight weakness of right arm and left leg; Babinski sign on left (?)
4	30 yr. ♂	4 mo.	Headache; dizziness; vomiting; fainting spells; dysarthria	Diplopia; impaired vision	Argyll Robertson pupils (inc.); paralysis of left external rectus; weakness of right external rectus; ptosis on right; papilledema	None	None noted	Cerebellar posture and gait; dysmetria and ataxia in left upper extremity	Hyperactive reflexes on right
5	37 yr. ♂	2 yr.	Headache; failing memory; impaired mentality	Diplopia; blurring of vision	Argyll Robertson pupils (inc.); limitations of upward gaze; right external rectus weakness; bilateral internal rectus weakness; papilledema	None	None noted	None	Bilateral hyperreflexia; right Babinski sign
6	20 mo. ♂	5 wk.	Vomiting; tonic spasms; coma	None	No strabismus noted; papilledema (?); child in coma	None	None noted	None	Decerebrate rigidity with absent reflexes
7	11 yr. ♀	5½ mo.	Headache; vomiting; nausea; drowsiness	Diplopia; impaired vision; tinnitus	Argyll Robertson pupils (inc.); weakness to conjugate deviation to right; ptosis on right; papilledema	None	None noted	Cerebellar posture and gait; athetoid movements of left hand; muscle rigidity on right	Weakness of left upper extremity

overlying tumor. In one case (case 2), softening in the midbrain created a new drainage channel and thus opened the way for the escape of cerebrospinal fluid into the fourth ventricle. This was followed by the disappearance of the papilledema that had been present earlier in the clinical course.

Microscopic Data.—In all tumors except one (cases 1 to 6) some phase of the basic pattern common to the developing pineal body during the first four months of postnatal life was found when the tumor was studied thoroughly. The pattern consisted of streams of small deeply staining cells which broke up the pineal territory into irregular circles or squares. These intermediate areas appeared as rarefied cellular aggregations in which the cells were large and of poor tinctorial qualities. When these two cell types were traced through the various stages in the developing pineal body, as well as through various areas in the pineal tumors, it was found that the large cells assumed the character of parenchymal cells, while the small cells were in some areas changing into fibrous tissue to become ultimately the supporting framework of the gland. In four instances (cases 3 to 6), in addition to the typical pattern, there were other architectural patterns which, though diverging from the basic morphologic features, were little more than imitations of either earlier or later phases in the development of the pineal body. In case 7, the histologic picture was an exact replica of a fully differentiated pineal body.

With the aid of special silver staining methods it was demonstrated that glial and nerve elements did not take part in the development of the pineal gland and did not contribute to the cellular structure of the pineal tumors.

The large multinuclear cells often seen in the tumors were found to be foreign-body giant cells in the majority of instances. They were commonly found in areas where regressive or involutional changes, such as calcification and fibrosis, were prominent.

GENERAL COMMENT

The observations recorded may now be evaluated in the light of the problem we began to investigate five years ago. At that time we had as material for study only two of the seven cases here reported. At the start it was our aim to find some basic architectural feature in these tumors and to establish their identity. As the material accumulated and as we familiarized ourselves with preceding contributions, it became necessary to widen the scope of our investigation so as to include tumors showing distinct structural differences though found in similar locations. A more systematic search for other histologic means of identification became imperative and led to the study of

histogenetic transitions in the postnatal evolution of the pineal body. This awakened our interest in the true nature of the histologic structure of this organ as revealed in its early development rather than in the stages when it has passed beyond the phase of full differentiation and entered a series of involutional alterations.

As the result of the various steps in this study, we have formulated some definite ideas about the structural character of this organ and about its relationship to the formation of tumors, and have assembled a few facts bearing on the supposed functions of the pineal body.

As regards its histologic structure, it would seem that its glandular character cannot be disputed, at least at some stage of its development. This is particularly striking at about the sixth month of intra-uterine life. Its cellular constitution and organization at that time point definitely to a glandular character. Tubules of various calibers are visible. In later stages of differentiation, a new feature, the rich vascularization, lays the foundation for an organ destined to perform an important function during a given stage in its evolution. This is emphasized by the relation of these vessels to the parenchymatous elements of the organ, a characteristic that is frequent in glands of internal secretion. Somewhat later, during the early days of postnatal life, another structural similarity to a gland of internal secretion, the suprarenal, appears, and is expressed in the rich blood supply, bordering on hemorrhage.

However, its glandular structure is only a part of a short transitional period. During the early months of postnatal life, it loses this structural character and assumes a new architecture, which does not permit of functional interpretation. Thus, it would appear that the glandular function is short lived, if one bases the assumption of its function on its histologic structure.

When we approach the problem of the histologic identity and derivation of these tumors we are on more firm ground. Here we find no difficulty in establishing a common histologic basis for tumors developed in the pineal region. We find a sound explanation for the divergence in the histologic pictures in a series of tumors arising in the same location. We can with certainty trace tumors, dissimilar as they appear to be in structure, to the same origin. In the microscopic make-up of the pineal gland in the third or fourth month of postnatal life, we find the histologic nucleus about which the variable histologic pictures of any tumor of the pineal type can be grouped. The identification of a tumor is readily made when its histology is matched with the microscopic picture of a stage in the development of the pineal body.

As to the question of the two main cell types so characteristic of this tumor, there is little choice left in the matter of assigning to the large clear cells a parenchymatous character and to the small cells the function of a supporting tissue. That the small cells are concerned

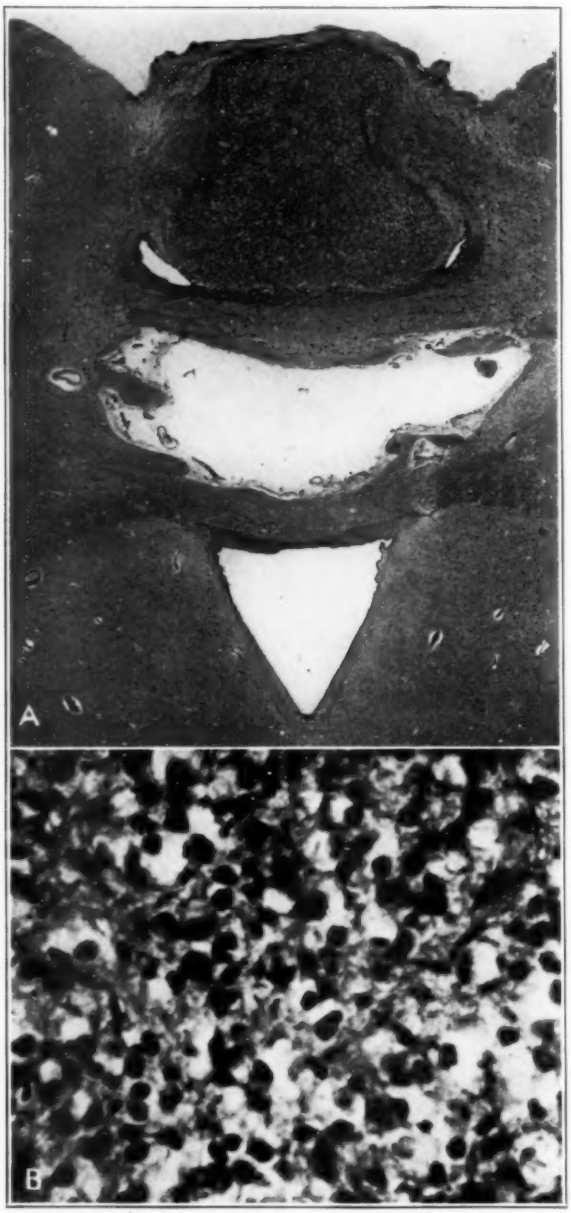

Fig. 44.—*A*, pineal rest overlying a cyst in the quadrigeminal plate. Hematoxyln-eosin; low magnification. *B*, section showing the microscopic structure of the pineal rest, shown in *A*. Hematoxylin-eosin; × 210.

with the formation of connective tissue cannot be doubted. The transformation of small cells into fibroblasts is clearly seen in some developmental stages of the pineal body (from 5 to 23 months of postnatal life). The formation of connective tissue stroma coincident with the disappearance of the small cells serves as additional evidence of this relationship. Also the presence of mast cells lends further support to the probable mesodermal character of these cells. In any event, this is a form of tumor that serves as an example of an autochthonous teratoid growth (Ewing[7]). It is a new growth of bidermal origin, with features of a true rudimentary organ, which is the result of a local disorder in development.

Of particular significance in connection with this study is the accidental discovery of a pineal rest in an apparently normal brain. It was found in the quadrigeminal plate on its dorsal aspect separated from the aqueduct of Sylvius by a cystlike structure (fig. 44*A*). Microscopic examination of this embryonal rest disclosed the structure of a pineal body in a fairly advanced stage of differentiation (fig. 44*B*), corresponding to the second year of postnatal development. This uncommon observation invites speculation as to the probable origin of the tumors under discussion. It raises the question whether similar embryonal rests do not serve as nuclei for the development of pinealomas.

SUMMARY AND CONCLUSIONS

1. Tumors of the pineal region in a group of seven cases are described.

2. The several tumors, though displaying individually divergent histologic pictures, are examples of a single type of new growth.

3. The identification of the true character of this type of neoplasm is aided by the study of the pineal gland through its various stages of development.

4. The pineal gland reveals several critical, histogenetic stages, which are duplicated by the histologic structure of tumors of the pineal region.

5. With the recognition of the architectural transitions in the developing pineal gland it is possible to assemble the majority of tumors of the pineal region, though diverging in histologic structure, into a single group.

6. The character of such tumors as autochthonous teratomas is established—and hence, the term pinealoma, as applied to such tumors, is placed on a firmer basis.

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7. Ewing, James: Neoplastic Diseases, ed. 3, Philadelphia, W. B. Saunders Company, 1928.

7. The absence of glial or neuronic elements during the evolutional stages of the pineal body excludes the existence of spongioblastic or neuroblastic forms of pinealoma.

8. Two distinct types of cells are found during the late prenatal and early postnatal development of the organ. As shown by the later postnatal changes and by similar alterations in tumors, the small, deeply staining cells are destined to form the supporting framework, while the larger cells constitute the parenchymal cells of the organ.

9. The cellular organization of the pineal body at an early stage of development points to its glandular character, at least for the brief prenatal period, and hence justifies its designation as the pineal gland.

10. The seven cases reveal no new or unusual clinical features, but add further support to the diagnostic criterion that in the presence of manifestations of increased intracranial tension the appearance of signs indicating involvement of structures in the periaqueductal region (external and internal ophthalmoplegia, skew deviation, impairment of upward gaze) justifies a diagnosis of tumor in the region of the quadrigeminal plate. In such event the lesion is most likely of the nature of a pinealoma.

11. The occurrence of alterations in the secondary sex characteristics (pubertas praecox) is not essential for the diagnosis of pinealoma. In our material only one case displayed such changes and only to a slight degree. In one instance manifestation of vegetative dysfunction (polyuria, polydipsia and somnolence) was present, but the effect of the obstructive hydrocephalus on the hypothalamic structures must be borne in mind in evaluating these symptoms.

ABSTRACT OF DISCUSSION

Dr. Frederick Tilney, New York: I wish to express my appreciation of the fine piece of work by Globus and Silbert. As you all know, there are today two distinct theories with reference to the pineal body. Dr. Bailey, no doubt, will ably espouse one theory, as he has on one or two occasions, but I am delighted to find so able an ally as Dr. Globus for the theory that I accept. Recently I have been working over this region rather incidentally, on some comparative vertebrate material, particularly in mammals, and I am more than ever convinced that the pineal body has definite glandular potentialities. In fact, I think that it is a plural potential organ if it is considered through all of its history from the beginning of its appearance in connection with the brain. It has the possibility of developing an eye, in fact, two eyes, and a series of racemose glands connected with the third ventricle by means of fine ducts, as in birds; it also has the possibility of developing a gland of internal secretion, which I think Dr. Globus has satisfactorily proved, at least for the early stages of life in man.

Dr. Percival Bailey, Chicago: I should like to surprise Dr. Tilney by saying nothing about the function of the pineal body, except to remark that I have not changed my former opinion expressed before this society.

I was rather surprised that Dr. Globus ignored the recent comprehensive studies of del Rio-Hortega, who showed clearly the presence of neuroglia in the pineal bodies of all kinds of mammals (Constitucion histológica de la glándula pineal: I. Células parenquimatosas, *Arch. de neurobiol.* **3**:359, 1922; II. Substratum neuróglico, ibid. **9**:26, 1929; III. Actividad secretora, ibid. **9**:139, 1929).

I should like to discuss the structure of the pineal tumors and in particular an aspect which Dr. Globus did not touch on in his presentation, but which occurs in the paper that he permitted me to read.

I am in agreement with the main thesis concerning the structure of these tumors. They are composed principally of large cells known as parenchymatous cells and smaller cells of mesenchymatous origin, and I think that I can add some data concerning their mesenchymatous nature.

The first slide shows a tumor from a boy of 13 years. You will notice the mass of large cells and, in between, other cells that are not lymphocytic but of the nature of mesenchyme.

The second slide shows that there is a great deal of reticulin which has been formed by these cells.

In another area of the same tumor (third slide) cartilage was actually formed by these cells, so concerning their mesenchymatous nature I do not take issue with Dr. Globus.

In Dr. Globus' paper he pointed out that he did not believe that spongioblastic and neuroblastic types of tumor could arise from the pineal body. I am sure that I have seen both. I have seen several tumors of spongioblastic nature, and I have also seen neuroglia cells in typical pinealomas.

The slide, for instance, shows a typical pinealoma composed principally of parenchymatous and connective tissue cells and a neuroglia cell with its fibrils running in every direction.

I also found a tumor of the pineal body which contained typical nerve cells (Horrax and Bailey: Pineal Pathology: Further Studies, ARCH. NEUROL. & PSYCHIAT. **19**:394 [March] 1928), and I am no longer willing to say that nerve cells cannot occur in the normal pineal body. I think no one would maintain that this is not a tumor of the pineal body. The whole region was cut in serial sections; there was no evidence of the pineal body with the exception of a little bean-shaped structure. It had the structure of a typical ganglioneuroma. Between the neurocytes was a certain amount of tissue composed mainly of spongioblasts.

The slide shows the nerve fibers scattered throughout the tumor. From my own experience I should say that the pineal body has the possibility of differentiating both neuroblastic and spongioblastic tumors, as well as the typical pinealomas that Dr. Globus so well described.

DR. JOSEPH H. GLOBUS: All of us will retain our own opinions as to the presence or absence of ganglion and glia cells in the pineal body. We all realize how difficult it is to be sure that the ganglion cells that form in a tumor of this type are part of the growth. One must bear in mind that tissue from structures adjacent to such tumors led to the error of accepting these cells as cells of the pineal tumor.

PAIN PATHWAYS IN THE SYMPATHETIC NERVOUS SYSTEM

CLINICAL EVIDENCE *

WILLIAM JASON MIXTER, M.D.
AND
JAMES C. WHITE, M.D.
BOSTON

The conception that sensory impulses are carried only by the cranial and spinal nerves has been held and taught for many years. Such a conception is hard to disprove. A corollary to this theory is that the sympathetic nervous system carries efferent motor impulses only. It must be admitted that the sympathetic nervous system has received but scant attention from the clinician in the past, and that the investigations of those interested in this system have frequently been passed over or contradicted without proper evidence. We shall present clinical evidence suggesting that sensory impulses may pass over pathways running in or intimately associated with the ganglia of the sympathetic chain and the white rami. Whether or not these pain-bearing pathways are somatic fibers running with the sympathetic nerves is unimportant if they can be interrupted by sympathectomy or the injection of alcohol. It may be that this clinical evidence suggests the blocking of some obscure sympathetic impulse rather than the interruption of a true sensory pathway.

The technic of investigation in the group of cases on which this report is based has been essentially the same. As a diagnostic measure (as previously reported by White [1]), we injected procaine hydrochloride into the ganglia that we believed played a part in the picture. If the result seemed satisfactory, the ganglia were removed, or alcohol was injected into them, or the communicant rami were severed.

Our present conception of the anatomy of these sensory pathways, if they really exist, may be stated briefly as follows: Pain-bearing nerve fibers probably run in many of the sympathetic nerves that course along the blood vessels of the head and neck. Whether these fibers are connected with the sympathetic ganglia of the head we do not know, but we believe that it is possible. We do not believe that any of these fibers

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* From the Neurological and Circulatory Clinics of the Massachusetts General Hospital, Boston.

* Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 9, 1930.

1. White, J. C.: Diagnostic Blocking of the Sympathetic Nerves to the Extremities with Procaine, J. A. M. A. **94**:1382 (May 3) 1930.

enter the central nervous system above the first dorsal segment, for there are no white rami above this level, and we believe that they may enter as low as the second and third. Pain pathways from the arm may enter through the sympathetic rami as low as the third and fourth dorsal. We think that pain from the aortic arch and the heart enters the spinal cord from the upper five or six dorsal sympathetic ganglia, and that it may reach the ganglia by two different routes: 1. One route is over the middle and inferior cardiac nerves to the cervical sympathetic trunk. As there are no white rami joining the cervical sympathetic with the cord, the pain fibers must descend at least to the first dorsal segment before they can enter the central nervous system. 2. A second set of gray rami run from the posterior cardiac and pulmonary plexuses

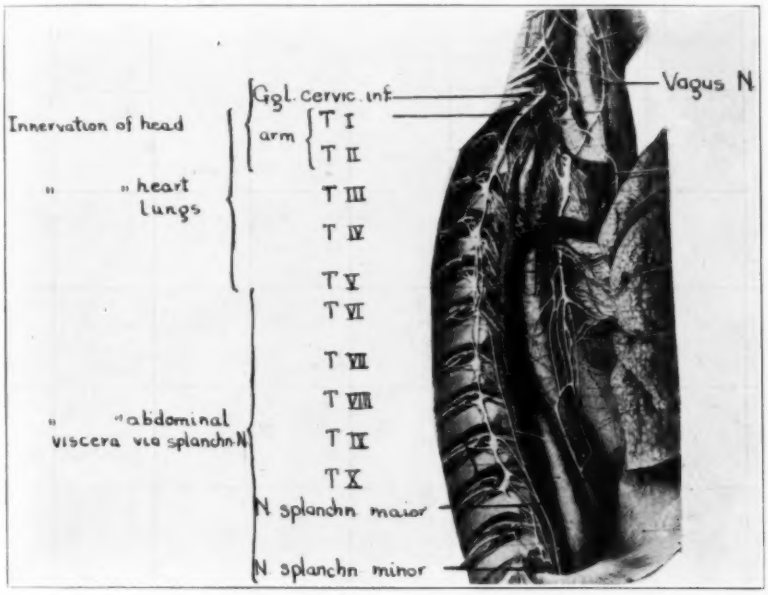

Fig. 1.—The sympathetic ganglia which must be removed to insure complete denervation of the head, arm, thoracic or upper abdominal viscera. The direct connections between the upper dorsal ganglia and the pulmonary and cardiac plexuses are also shown. Adapted from Braeucker, W.: Der Brustteil des vegetativen Nervensystems und seine klinisch-chirurgische Bedeutung, Beitr. z. Klin. d. Tuberk. **66**:1 (March) 1927, Berlin, Julius Springer.

directly across the posterior mediastinum to the second, third, fourth, and sometimes to the fifth and sixth ganglia. These low cardiac connections have been shown by Jonesco and Enachesco,[2] by Braeucker,[3]

2. Jonesco, D., and Enachesco, M.: Compt. rend. Soc. de biol. **97**:977 and 980, 1927.

3. Braeucker, W.: Der Brustteil des vegetativen Nervensystems und seine klinisch-chirurgische Bedeutung, Beitr. z. Klin. d. Tuberk. **66**:1 (March) 1927.

and by Kuntz.[4] Their functional importance has been shown by Cannon, Lewis and Britton [5] and by Singer and Spiegel.[6] We have had little experience with pain pathways from the upper abdominal viscera, but it is our belief, from the course of the splanchnic nerves, that pain from this region enters the cord in the dorsal region probably from the fifth dorsal to the first lumbar sympathetic ganglia.

This anatomic conception explains, we believe, the failures experienced in earlier operations devised for relief from cardiac pain and is the basis of our own attempts to give relief from certain types of pain in the head, arm, thorax and upper part of the abdomen.

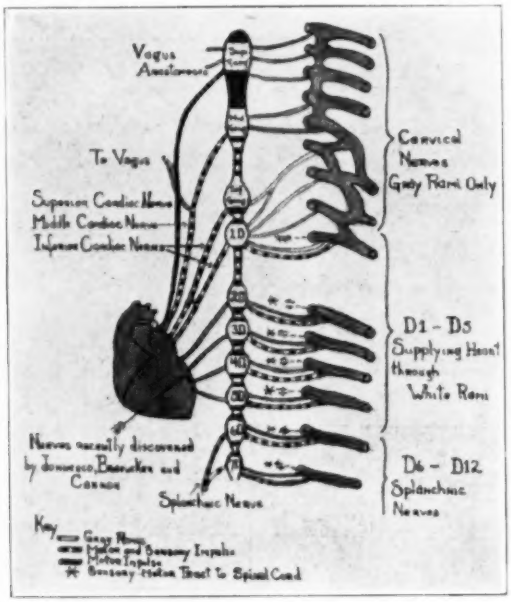

Fig. 2.—Diagram to show the connection between the central nervous system with the cervicodorsal sympathetic trunk and the nerves running from the trunk to the heart. The nerves described by Braeucker, Jonesco, Enachesco and Cannon, connecting the upper dorsal ganglia directly with the heart, are sketched in outline.

4. Kuntz, A.: Distribution of Sympathetic Rami to the Brachial Plexus, Arch. Surg. **15**:871 (Dec.) 1927.

5. Cannon, W. B.; Lewis, J. T., and Britton, S. W.: A Lasting Preparation of the Denervated Heart with Evidence for Accessory Accelerator Fibres from the Thoracic Sympathetic Chain, Am. J. Physiol. **77**:326, 1929.

6. Singer, R., and Spiegel, E. A.: Der Weg des Herz- und Aortenschmerzes über die Hinterwurzeln zum Zentral Nervensystem, Ztschr. f. d. ges. exper. Med. **55**:607, 1927.

REPORT OF CASES

Atypical Neuralgias of the Face.—Two patients were studied and submitted to operation. In both cases the posterior root of the trigeminal nerve had previously been cut with only temporary relief, and in one the glossopharyngeal nerve, superior cervical ganglion and the periarterial sympathetic nerves of the carotid had been removed as well. Both patients suffered from severe burning pain coming in attacks that lasted several hours. The pain was deep-seated and extended beyond the distribution of the fifth nerve, involving the ear, back of the head and side of the neck. There was marked hyperesthesia in the painful areas, the reaction in the area supplied by the fifth nerve being obtained by deep pressure or by heat or cold. Both patients showed pain on pressure over the great vessels of the neck. Cocainization of the sphenopalatine ganglion was without effect, but com-

Fig. 3.—Causalgia of hand and arm. Distribution of pain following traumatic amputation of index finger. From White, J. C.: Am. J. Surg. **9**:264 (Aug.) 1930, New York, Paul Hoeber, Inc.

plete relief from pain was obtained for several hours after injection of procaine hydrochloride into the cervicodorsal and second dorsal ganglia. We operated on both patients, employing the technic suggested by Henry [7] and developed by Adson [8] for relief of Raynaud's disease and allied conditions in the upper extremity. In one case, the whole cervicodorsal and the second dorsal ganglia were removed, with complete relief, which has now persisted nearly three months. In the other,

7. Henry, A. K.: A New Method of Resecting the Left Cervico-Dorsal Ganglion of the Sympathetic in Angina Pectoris, Irish J. M. Sc. **5**:157 (April) 1924.

8. Adson, A. W.: The Treatment of Raynaud's Disease by the Resection of the Upper Thoracic and Lumbar Sympathetic Ganglia and Trunks, Surg. Gynec. Obst. **48**:577 (April) 1929.

the first patient operated on, the lower portion only of the cervicodorsal ganglion and the second dorsal ganglion were removed. The result was interesting but unsatisfactory. Pain and hyperesthesia of the ear and occipital region seemed to be almost entirely relieved, but the patient continued to complain of severe pain in the face. Reinjection with procaine hydrochloride again gave temporary relief, and the patient was operated on again. Unfortunately, owing to the amount of scar tissue caused by the first operation, the remains of the cervicodorsal ganglion could not be found, and the patient still suffers a great deal of pain. This operation has been performed successfully for atypical neuralgia of the face by Frazier and Grant,[9] in Philadelphia, and by Flothow,[10] in Seattle.

Since operating in these two cases, we have injected the procaine hydrochloride into the cervicodorsal ganglion in four cases of apparently typical neuralgia of the

Fig. 4.—Aneurysm of the arch of the aorta. Distribution of pain; *1* and *2* mark points where alcohol was injected paravertebrally under the first and second ribs. From White, J. C.: Am. J. Surg. **9**:264 (Aug.) 1930.

face, with rather surprising results. In two, the temporary relief from pain was complete, and in the others relief was from 50 to 75 per cent. Two of these patients were relieved by subsequent injection of alcohol into the appropriate nerve trunks, according to Patrick's technic; one patient refused any operative procedure or injection with alcohol, and we expect to operate on the other patient in the near future and remove the cervicodorsal and second dorsal ganglia. We

9. Frazier, C. H., and Grant, F. C.: Personal communication.

10. Flothow, P. G.: Discussion on paper by Adson and Brown: Thoracic and Lumbar Sympathetic Ganglionectomy in Peripheral Vascular Disease, J. A. M. A. **94**:252 (Jan. 25) 1930.

are unable to explain the results and realize that confirmation of this observation is necessary.

Causalgia of the Hand.—The patient was a man, aged 30, whose right index finger was crushed in a box-making machine in May, 1929. The finger was amputated through the middle phalanx. When he came to the hospital he had a cold, painful hand with pain running up the inner side of the arm deep into the chest. Peripheral diagnostic injection failed to relieve the pain, whereas paravertebral injection into the two upper dorsal ganglia gave complete success. These two ganglia were removed by Dr. A. W. Allen and one of us (J. C. White) on Feb. 7, 1930, with complete relief from pain to date.

Aneurysm of the Aortic Arch—Syphilis.—A man, aged 48, entered the hospital fifteen months ago with a huge aneurysm of the ascending arch of the aorta pushing up between the clavicle in front and the first rib behind. The lesion was causing a paroxysmal brassy cough and constant pain extending from the top of the head to the fourth rib on the right. We reasoned that the pain must be of sympathetic origin as the cervical spinal nerves could not possibly be involved. A test injection of procaine hydrochloride into the region of the first and second

TABLE 1.—*Comparison of Two Methods of Treatment* *

		Paravertebral Alcohol Block	Cervical Sympathectomy	
			Total	Partial
Number of cases		21	66	116
Relief	Good, 100% to 50%	71.5%†	58%	53%
	Improved, 50% to 25%	9.5%	13.4%	22%
	Failures, 25% to 0	19.0%	7.6%	13.5%
Deaths		0	21%	7.5%

* The patients in our group of cases were treated by injections of alcohol, and in those cases collected from the literature cervical sympathectomy was used.
† Two cases observed too short a time to be certain of results.

intervertebral foramina on the right was temporarily successful. Five cubic centimeters of 95 per cent alcohol was therefore injected at each of these points and gave complete relief from pain until death three months later from rupture of the aneurysm. Autopsy showed an effective block of the first and second communicant rami. We are unable to explain this case on any grounds other than that the pain sensation entered the cord over these two rami and was referred to the distribution of the cervical and upper dorsal nerves.

Angina Pectoris.—To date, we have treated nineteen patients with angina pectoris by injection of alcohol and four by dorsal ganglionectomy. The results obtained by injection are well shown in the accompanying table and hardly need any comment. Our method is similar to that described by Swetlow [11] except that diagnostic injection of procaine hydrochloride is used first in cases in which we have any doubt as to the proper ganglia into which the injection should be made.

It is our opinion that injection of alcohol cannot be as sure as ganglionectomy, and for that reason four patients have been submitted to dorsal ganglionectomy. Here, as in the lesions of the head and arm, we have used the dorsal approach. The anatomic and physiologic proofs of

11. Swetlow, G. I.: Paravertebral Alcohol Block in Cardiac Pain, Am. Heart J. **1**:397 (April) 1926.

the existence of cardiac fibers running to the dorsal sympathetic ganglia are so convincing that we have come to believe that the old operation of cervical sympathectomy should be given up in cases of cardiac pain. Operation through the neck cannot possibly interrupt the direct sensory pathways in the mediastinum. This is doubtless why Jonesco's operation failed to give satisfactory relief in 40 per cent of cases of angina pectoris. Only if one removes the upper dorsal ganglia or their communicant rami or injects alcohol into them can he be sure of obtaining the desired result.

One possible objection to this method of attack has to be faced—in removing all the sensory cardiac fibers the accelerator nerves to the heart may also be paralyzed. We have seen no evidence of cardiac decompensation in these cases. Leriche,[12] Danielopolu,[13] Braeucker [3] and others claim that the capacity of the heart is greatly diminished. On the other hand, Cannon, Lewis and Britton [5] have shown that the desympathectomized heart can still be accelerated by the secretion of the suprarenal gland and by the reduction of vagus tone. Jonesco and Raileanu [14] have found no evidence of cardiac degeneration on histologic examination. Lastly, Lampert [15] has removed both stellate ganglia in dogs and has then run them hard behind a horse for distances up to 15 kilometers without causing evidence of unusual fatigue.

All four cases of angina pectoris in which operation was performed, including one in which the surgical work was done by Dr. A. W. Allen, were chosen because the patients had fair life expectancy and extremely severe left-sided angina. All four of the patients felt that they would take any risk for complete cure on account of various social reasons rather than take the risk of failure from the use of alcohol. We believe that this risk cannot be avoided in 25 per cent of cases and that it is due to the technical difficulties of absolute accuracy in injection. All were completely relieved from all left-sided pain. One is living and well eight months after the operation. Another died nine months after the operation of severe right-sided angina and probable coronary occlusion, and the third died ten days after the operation with severe right-sided angina. Autopsy in this case showed nothing to indicate that death was due to the operation, but did reveal that the left coronary artery was completely occluded and 50 per cent of the right artery shut off. The last case must properly be classed as an operative death as the patient developed postoperative pneumonia, and when he died five weeks

12. Leriche, R.: La chirurgie de la douleur, Presse méd. **35**:497 (April 20) 1927; Résultats de la chirurgie de la douleur, ibid. **35**:561 (May 4) 1927. Since this article has been in the press, Leriche has modified his views and concluded that even bilateral removal of the stellate ganglia is well supported. (La chirurgie de la ganglion étoilé et ses bases expérimentales, Bull. et mém Soc. nat. de chir. **54**:864 [June 18] 1930.)

13. Danielopolu, D.: L'angine de poitrine et l'angine abdominale, Paris, Masson et Cie, 1927.

14. Jonesco, D., and Raileanu, C.: Effect of Extirpation of Stellate Ganglion on the Myocardium, Wien. Arch. f. inn. Med. **19**:199 (Nov. 14) 1929.

15. Lampert, F.: Experimentelle Beiträge zur Denervation des Herzens, Arch. f. klin. Chir. **155**:597, 1929.

later of coronary thrombosis, a small interlobar abscess was also found which may have contributed to the fatal outcome.

Thoracic and Gastric Crises of Tabes Dorsalis.—This patient had had severe lightning pains in the left lower ribs and abdomen for four years. He was addicted to morphine and had had three previous operations. The first and second operations were chordotomy on both sides; they were not complete as shown by the sensory examination. The third operation was section of all posterior roots from the fifth to the tenth dorsal, inclusive. There was complete anesthesia to pin prick and light touch and he could not recognize heat and cold. Deep pressure sensation was preserved and cold caused exacerbations of the pain. Paravertebral injection of procaine hydrochloride, from the seventh to the eleventh dorsal inclusive, relieved all pain for twenty-four hours and made the abdominal wall completely anesthetic. He was operated on, and the sympathetic chain was exposed. The seventh to the ninth ganglia were removed and through the same

TABLE 2.—*Dorsal Ganglionectomies in Angina Pectoris*

Case	Age	Diagnosis	Operation	Results
1	18	Rheumatic heart disease; aortic regurgitation; up to eighteen attacks of angina at rest daily, severe on left, mild on right	Resection D_1-D_2 2/5/29	Complete relief of left-sided pain; return to active work; died at nine months of right-sided attack
2	29	Syphilitic aortitis; three to four attacks daily; severe attacks of left-sided angina	Resection D_1-D_3 9/19/29	Good recovery and no more pain; died suddenly on eleventh day with severe right-sided pain; autopsy showed total occlusion of left coronary artery, 50 per cent occlusion of right coronary
3	57	Rheumatic and hypertensive heart disease, severe angina on left, mild on right	Resection D_1-D_3 10/1/29	Total relief on left; still has mild right-sided attacks
4	62	Arteriosclerotic heart disease with coronary thrombosis and angina pectoris	Resection D_1-D_3 injection of alcohol D_4-D_6 3/19/30	Total relief of angina; postoperative pneumonia; died 1 month later of coronary thrombosis; small area empyema found at autopsy

incision the great splanchnic nerve was exposed and a segment of it removed. This put an end to the left-sided abdominal pain. After this he began to notice deep pain in the chest which had been submerged in the more severe abdominal pain. This was controlled by diagnostic injection of procaine hydrochloride into the fourth to the seventh rami. Relief was also obtained from this pain, but in a slightly different manner, as we used the von Gaza [16] operation in which the communicant rami are severed close to the intervertebral foramina. This operation has been used successfully by a number of operators to control upper abdominal pain, notably Leriche and Fontaine,[17] van Bogaert and Verbrugge,[18] Archibald [19]

16. von Gaza, W.: Die Resektion der paravertebralen Nerven und die isolierte Durchschneidung des Ramus communicans, Arch. f. klin. Chir. **133**:429, 1924.

17. Leriche, R., and Fontaine, R.: La chirurgie du sympathétique, Rev. neurol. **1**:1046, 1929.

18. van Bogaert, L., and Verbrugge, J.: Pathogenesis and Treatment of Gastric Crises of Tabes by Neuroramisectomy, Surg. Gynec. Obst. **47**:543, 1928.

19. Archibald, E.: Effect of Sympathectomy for Obscure Pain, Tr. Am. Surg. A. **46**:179, 1928.

and Scrimger.[20] We believe that it has never been used for the thoracic crises of tabes, and that intrathoracic section of the great splanchnic nerve has not been performed before.

SUMMARY AND CONCLUSIONS

We have presented experiences with patients suffering from the severest types of pain who were relieved by interruption of the dorsal sympathetic fibers. We realize that this group of thirty-one cases is too small, and that the patients have been treated too recently for us to draw any far-reaching and definite conclusions. To the best of our knowledge, removal of the upper thoracic ganglia for these painful conditions has rarely been reported heretofore. The evidence so obtained, together with that gained from diagnostic block with procaine hydrochloride and injection of alcohol has led us to believe that there may be definite sensory pathways running in the dorsal sympathetic chain. We hope that this report will stimulate other surgeons to make further observations on these baffling painful conditions and that they will publish their conclusions concerning the existence of these pathways and the method of attack.

ABSTRACT OF DISCUSSION

Dr. Lewis J. Pollock, Chicago: I am gratified that we have some additional procedure to serve in relieving many of these painful disorders. I think, however, that it is dangerous to come to a conclusion as to a physiologic principle from such clinical observations. For example, I wonder whether the disappearance of spontaneous pain actually means an interruption of a sensory pathway. Is it not more rational to suppose that one should insist on the development of sensory loss, certainly to some degree and to some type of sensibility, following such an interruption of the sympathetics if they serve as a pathway? For example, it is well known that a hot water bag will stop toothache in some instances, yet I doubt very much if there is an interruption of any sensory pathway; it is exceedingly likely, it seems to me, that there may be some intermediate mechanism at work, which may be responsible for pain, that may be affected by an interruption of the sympathetic nervous system but that has nothing at all to do with the sensory pathway. I noted that in one of the illustrations there was a diagram as if there had been a sensory examination; if there was a loss of sensation, was that explained by Dr. Mixter on the basis of an interruption of the sympathetics, or was there not an inclusion of the peripheral nerve?

Dr. Francis C. Grant, Philadelphia: It is extremely difficult to obtain relief from atypical neuralgic pains in the face. They seem to be precisely similar, whether they come on spontaneously or whether they follow an operation for avulsion of the sensory root of the fifth nerve. Of course, one of the probable reasons why these pains are similar, whether they appear spontaneously or follow operation, is the fact that an error in diagnosis is made, the pain being atypical from the beginning, and operation fails to give relief or to change the character of the pain. In Dr. Frazier's clinic we have attempted many times to obtain relief

20. Scrimger, F. A. C.: On the Possibility of Relieving Abdominal Pain by Section of the Sympathetic Rami Communicanti, Canad. M. A. J. **21**:184 (Aug.) 1929.

from these atypical pains by stripping the sympathetic sheath of the common carotid artery and by avulsion of the superior and middle cervical ganglia in the neck.

Based somewhat on Dr. White's work, we have also attempted paravertebral injections for relief from pain. In one of two cases, injection of procaine hydrochloride into the region of the first and second thoracic ganglia promptly produced a Horner's syndrome on the side on which the injection was made and relief from pain resulted. In a second case, injection was apparently less effectively given, and relief did not appear so promptly or completely. The patients in these two cases have been subjected to thoracic ganglionectomy. In the first case in which the infiltration with procaine hydrochloride proved so successful, the patient was relieved from pain and has remained so for twelve months. In the second case, in which we thought that the injection had not been so effectively given, relief was obtained for about three months, and now we learn that the pain has returned with almost its original severity.

It seems, therefore, that cases of atypical neuralgia which have been so intractable to any form of relief in the past can be helped by thoracic ganglionectomy provided that relief can be obtained by injection of procaine hydrochloride into the neighborhood of the ganglion. The effectiveness of the injection should be the criterion on which to base a decision for an operative intervention.

Dr. Walter Timme, New York: I wish to stress the nature of the pain as related to those structures accredited to the sympathetic ganglia as distinguished from pain carried by the ordinary nerves. In structures controlled more or less in their activity by the sympathetic, pain is not produced by cutting or injury; witness the possibility of painless operative procedures on an intestine without any anesthetic. Pain in those structures is produced by spasm as a rule, and it is the relief from that spasm, which I think Dr. Pollock possibly maintains, that is the groundwork for the relief from pain.

The avulsion and destruction of high dorsal ganglia of the sympathetic chain which are responsible for spasm of certain vessels, producing by their contraction pain in their vicinity with acrocyncope, simply give relief from the spasm and from the pain incidental thereto.

Dr. Alfred W. Adson, Rochester, Minn.: I have never operated on a patient with the atypical pains that have been referred to, but I have had occasion to do a large number of cervical thoracic ganglionectomies. We had one patient who had a ganglioneuroma in the first thoracic ganglion which was diagnosed, explored, found and removed; relief was obtained from the pain by resecting the first and second thoracic ganglia with the tumor.

I have often seen marked relief from pain in thrombo-angiitis obliterans of the upper extremities following a cervicothoracic ganglionectomy. The relief obtained in angina pectoris by this operation, by the Jonesco operation and by the resection of the superior cervical ganglion is probably due to vasomotor release of the coronary arteries as well as due to section of afferent pain fibers. I have changed the original operation of cervicothoracic ganglionectomy and enter the thorax through the first rib instead of the second, since it permits a more complete removal of the lower cervical ganglion with the first thoracic ganglion and also facilitates a thorough dissection of the first thoracic spinal nerve, thus minimizing the chances of missing both afferent and efferent sympathetic fibers.

Dr. Bernard Sachs, New York: Like many others, I have always felt great responsibility in the treatment of patients with angina pectoris, and while I am deeply interested in the theoretical considerations as to the exact manner in

which the sympathetic ganglion may possibly influence the condition, I would like to ask this: Have we reached the point at which we can recommend these surgical endeavors with reference to the duration of life, the probable duration of life and the intensity of the disease? In angina pectoris, the majority of cases at any rate occur in persons of far advanced years.

I noticed, if I was correct in interpreting the tables that were given, that 21 per cent of the patients in cases of total ganglionectomy died. Is the immediate risk of the operation very great? Also, under what anesthesia were these operations performed? Is the immediate risk so great that one has to decide whether life is going to be prolonged or whether there is danger of early death, and then, of course, whether the patient prefers early death to the continuance of the severe symptoms? The surgical treatment of such a precarious condition as angina pectoris is of great importance, and I should be glad if one could have a little more light on that question from the more practical point of view, that is, the point of view of the physician who is asked what he is to do in the case of angina pectoris in a man or woman of advanced years.

Dr. Charles R. Ball, St. Paul, Minn.: Having come in contact with many of these patients and having had the opportunity of observing them carefully, I have long thought that the painful reactions of patients with tic douloureux were due perhaps to a central condition rather than to a local one. Last fall, while making an injection into a patient who was a bleeder and who had severe tic douloureux, severe hemorrhage resulted without any relief from pain. I had given him an injection on a previous occasion with relief for about two years. I remembered that once previously in a severe case with early return of pain following a deep alcoholic injection I had seemed to have obtained some benefit by fever therapy. I decided to give this patient an intramuscular injection of milk and secured a sharp chill with a marked fever reaction. After two such injections, the pain stopped entirely. This was in October, 1929, and he has been free from pain since.

I have treated eleven patients in this way with rather astonishing success in the relief from pain. How permanent this will be, I do not know. In some cases in which the fever reaction was not marked, the pain returned, but by securing a more marked reaction it disappeared.

Dr. White: It is difficult to answer Dr. Pollock's question because, of course, the sympathetic ganglion has no skin manifestations by which one can test whether sensory block has been achieved, but we have two cases that throw some light on this. One was a case about which Dr. Mixter did not speak. The patient suffered from tabetic crises that involved both the entire left side of the abdomen and the left side of the thorax. He had had all of the left posterior roots cut from the sixth to eleventh thoracic segments. That had failed to give relief from the pain, and he then had a chordotomy, which produced anesthesia in the leg but did not give relief from the gastric crises. Following these procedures it was possible to stick a pin anywhere in the left side of the abdomen but not to touch him with ice, rub gauze over the area or press deeply, without causing intense spasm and pain. Procaine hydrochloride was then injected into all the sympathetic roots, and for the first time he was completely desensitized; it was possible to apply cold, heat or pressure and there was no pain whatsoever. As a result of this test, the left splanchnic nerve was removed and the seventh, eighth, ninth and tenth dorsal sympathetic ganglia were resected. This gave permanent loss of the hyperesthesia and gastric crises. At a second stage, the third to sixth sets of communicant rami were resected on the left, which has put an end to the thoracic crises of pain for nine months.

The second case was that of a patient, of whom Dr. Mixter spoke, who had trigeminal neuralgia and an area over the side of the face, scalp and neck where she was intensely hypersensitive to cold and pressure after the posterior root of her gasserian ganglion had been cut. With injection of procaine hydrochloride this hyperesthesia disappeared, and with the cutting of the sympathetic fibers to the head she has been permanently relieved. This fact is difficult to account for, except on the basis that certain types of pain can be carried over sympathetic fibers, because all the anatomic pain tracks to the face had supposedly been cut and yet all types of pain sensation were not interrupted and were not relieved until the cervicodorsal and second dorsal ganglia were resected.

Dr. Adson spoke of the relief from angina pectoris being due probably to a motor effect by preventing spasm of the coronary arteries. That may be true in angina, there is no way of telling, but in the patient with the aneurysm it seems difficult to believe that pain was due to any type of spasm, because the pain was constant; there was a big dilated aneurysmal sac and the pain was present constantly for several months. With diagnostic infiltration of procaine hydrochloride into the region of the upper two dorsal vertebral foramina and again following injection of alcohol, permanent relief from the pain was obtained.

Dr. Mixter: Concerning the question of the practical application of injection of alcohol, or removal of the ganglion in angina pectoris, we chose these cases carefully from a large number of cases of angina pectoris. We have not operated or used injection of alcohol in any case in which the patient could get along with any ordinary medical treatment for angina. Practically all of the patients who have been treated surgically have been patients that have had anginal attacks while lying quietly in bed. Some of the patients have been elderly people; some have been of middle age, and one or two have been young. One was a boy with a bad rheumatic heart. He was only 22 or 23 years of age.

We have chosen for injection with alcohol the cases in which life expectancy seemed to be shorter than in those in which we chose operative means. The technical difficulties of injection with alcohol are such that one must face a certain definite error due to inability actually and accurately to inject the alcohol into the ganglion. We have set that error, owing to our failures, at 25 per cent. In the group of cases of injection with alcohol we had no deaths, and one patient is now alive and in good condition three years after the injection.

In the operative cases we have used surgical means in cases in which for some reason the patient did not wish to take the chance of a 25 per cent possibility of failure. We have thought that an operation following an injection of alcohol would probably be impossible on account of the formation of scar tissue.

I think that the injection of foreign protein in trigeminal neuralgia is of interest and I shall be glad to give it a trial.

PHYSIOLOGIC DIFFERENCES BETWEEN GENERIC AND INDIVIDUALLY ACQUIRED AUTOMATIC ASSOCIATED MOVEMENTS*

L. VOSBURGH LYONS, M.D.
AND
RICHARD M. BRICKNER, M.D.
NEW YORK

It is not our purpose to enter a disputatious field. We shall not, at the moment, concern ourselves with the essential nature of volition, motion or any other contemporarily insoluble issue. While the basic character and even the existence of the so-called automatic associated movements are admittedly in dispute, we believe that a working definition of them can be given.

By associated movements we mean those resulting from the combined action of different groups of muscles producing simultaneous and related motion of two or more well separated parts of the body, such as the two arms. Prime examples are the normal swinging of the arms, which is a part of walking, and the motions of one leg as related to those of the other in walking. Such phenomena as the extension of the wrist during grasping do not fall definitely into the group we are considering. In our use of the word automatic we wish expressly to avoid making any interpretation of the conception of volition. By the associated movements that are automatic, we merely refer to those that can be performed in proper synchrony without direct, attentive, conscious guidance; in other words, those movements that can be well executed while the attention is centered almost entirely elsewhere.

It is common clinical experience that some movements that fall into this class are, if not lost, at least poorly executed in paralysis agitans.

We believe that there is considerable evidence that these impairments do not depend wholly on the rigidity.[1] The poverty of facial movement during the play of such emotions as laughing and crying might indeed be caused in the main by rigidity, but we do not understand how rigidity can account for the relative absence of facial expres-

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* From the Neurological Institute of New York and the City Hospital.

1. Wilson, S. A. K.: Disorders of Motility and of Muscle Tone, Lancet **2**:1, 53, 169, 215 and 268, 1925. Foerster, O.: Ztschr. f. d. ges. Neurol. u. Psychiat. **73**:1, 1921.

sion during rest. It is also true that there are many parkinsonian cases —early ones, especially—in which the arms do not swing during walking, but in which little or no rigidity can, at the time, be demonstrated. Moreover, in some cases of Sydenham's chorea there is impairment of such associated movements as swinging of the arms. Yet it is common knowledge that there is no rigidity in this condition. It can hardly be denied that there must be some sort of anatomic patterning behind the coordinating of complex movements which can be executed without full attention, and it seems fair to reason that disturbed execution discloses a derangement of this patterning. Emphasis alone on slowness, fatigability and weakness leads perforce to undue emphasis on the factor of rigidity. We do not believe that such considerations are concerned with the totality of integration. On the other hand, such elements as grace do reflect the degree of this totality. Preservation of grace, despite weakness, shows that there may well be something specific about the pattern for any particular associated movement.

We wish to present an observation which, we believe, is added evidence that such patterning exists in a specific way, and that the disturbance of certain performances in parkinsonism rests on a more profound basis than rigidity alone.

Simply stated, this evidence consists entirely in the observed preservation of grace and ease (in the face of weakness and rigidity) in the execution of certain specific actions in patients with well marked parkinsonism.

Our notice was first directed to this matter by the behavior of a patient at the City Hospital, New York. He had been a star pitcher for the New York Giants until six years before, when he contracted definite and typical epidemic encephalitis. Parkinsonism gradually developed, and for the last two years he has shown a fairly extreme picture of that condition. He is able to walk, but with difficulty, and all his routine motions are made with the usual retardation. In our test the man stood on the lawn of the hospital, his head and shoulders stooped, his hands trembling, his whole attitude one of characteristic rigidity and immobility. But when a ball was thrown to him, his whole body immediately became plastic; he made a perfect catch out at the side, and at once threw the ball back. The whole act was characterized by a beauty and grace not attainable by the ordinary normal man. The movements were perhaps slightly slowed—a factor which we attributed to rigidity. The observation was repeated many times, and is shown in figures 1, 2 and 3.[2]

2. During the reading of this paper, the throwing and catching were demonstrated in moving pictures.

Fig. 1.—View of the catching position, showing the graceful mobility of the patient in making a rapid change of position. Note the position of the left arm and leg.

Fig. 2.—In the figure on the left the ball has just been caught in a position somewhat above the level of the patient's head. In the figure on the right, the ball has just been caught in a position above and considerably outward from the patient's left knee. Note especially the ease and evident speed of the patient's movements.

Fig. 3.—View of attitude taken by the patient during the throwing of a ball. Note the grace and mobility which are evident in his movements.

It is the experience of many observers that some few other coordinated activities can be very well performed (under usual rather than exceptional conditions) by rigid parkinsonian patients. Of these, dancing is the most striking and common. We are also acquainted with a patient who, despite severe parkinsonism, has retained a very good golf stroke, and another whose automaticity in driving an automobile is relatively unimpaired.

One can separate those associated and relatively automatic movements that are seriously impaired in parkinsonism from those that are well preserved from the standpoint of grace and evident ease. The distinction does not apply, of course, to slowness, fatigability or weakness. It is fully admitted that the preserved functions are the fewer. The accompanying tabulation lists some of both types of function:

Usually Much Impaired in Grace and Ease	*Occasionally Little Impaired in Grace and Ease*
Swinging of arms in walking	Dancing
Use of larynx in making modulated sounds	Golf strokes
Coordinated use of auxiliaries in sitting and arising	Facility in driving an automobile
Lack of facial expression at rest	Catching and throwing a ball

If the two groups are contrasted, it is seen that the heavily impaired functions are those that are clearly phylogenetically grounded, while those whose grace is preserved are just as obviously individually learned. We have thus been led to the following hypothesis: We know that certain movements, which are both automatic and associated in the sense we have defined, must depend on some type of anatomic patterning in the central nervous system. Allowing in full for the effects of rigidity, the grace of some of these movements is seriously disturbed in parkinsonism, while that of others is left relatively untouched, and thus a clearcut differentiation can be made between the two. Since the lesions in Parkinson's syndrome are most constantly and frequently found in the corpus striatum, it seems almost inescapable that the perfect patterning of many of the phylogenetic automatic associated movements is a striatal function, while that of the individually acquired ones is a process of some other part of the brain, presumably some part of the cortex. It does not appear likely that both are mediated through the cortex, because, if the lesions causing parkinsonism are sufficiently widespread to impair phylogenetic movements by cortical involvement, it is strange that the personally acquired ones should so frequently escape. At least, the controlling regions must be so far separated that dissociated impairment can occur.

It might be said that the ability to run—obviously phylogenetically founded—is frequently preserved in parkinsonism, and that this and perhaps some other similar facts point against the validity of the

hypothesis. However, in this preservation, there is neither ease nor grace. It is probably related to maintenance of balance. Moreover, the existence of such a preservation, even if it included grace and ease, would not vitiate the fact that there exists a group of individually learned movements that can be contrasted with phylogenetically fixed ones.

REPORT OF CASE

History.—F. B., aged 50, was admitted to the City Hospital, New York, July 2, 1924, complaining of trembling of the hands and legs. In the winter, 1923, he had had a severe illness with fever, during which he was lethargic most of the time. Six months later he had intermittent diplopia, which lasted six months. About a year later trembling of the hands and legs appeared; these, as well as generalized weakness and rigidity, have progressed steadily.

The patient had had malaria in 1914. He was a pitcher for the New York Giants in 1902.

Examination.—The facies was masked, and there was a typical parkinsonian attitude. The gait was slow and shuffling, and the arms did not swing. Saliva drooled from the mouth. The characteristic parkinsonian tremor was present, involving the hands and legs. There were generalized muscular rigidity and weakness.

The deep and superficial reflexes were normal; the cranial nerves were normal except for tremor of the tongue.

SUMMARY

1. Attention is called to the existence of a group of automatic associated movements that are individually acquired, and that can be contrasted with those that are phylogenetically grounded.

2. The latter group is seriously impaired in Parkinson's syndrome, while the former may escape. Thus we have added evidence that both groups depend on some type of anatomic patterning.

3. Therefore, the rigidity alone cannot account for the impairment of movement in parkinsonism, and this again shows that the patterning of phylogenetic automatic associated movements is a striatal function.

4. The patterning of the individually acquired movements is, presumably, a function of some part of the cortex.

THE SYNDROME OF THE BRACHIUM CONJUNCTIVUM AND THE TRACTUS SPINOTHALAMICUS *

COLIN K. RUSSEL, M.D.
MONTREAL, CANADA

If an excuse is needed for presenting a single case, the anatomic and physiologic interest which this case bears is sufficient.

REPORT OF CASE

History.—J. W., aged 67, a caretaker and furnace man, was admitted to the hospital on April 1, 1929, complaining of headaches and dizziness. About five months before, he had begun to suffer from attacks of headaches and dizziness, which usually occurred when he was at work. He would suddenly become dizzy, vision would become blurred, and he would have to support himself to keep from falling. There was no loss of consciousness and at first no vomiting. No peculiar sensations occurred in the body or limbs, and there was no muscular weakness. The attacks would last from ten to fifteen minutes and immediately pass off if he sat or lay down. The attacks had been becoming more frequent and more severe, and the headaches were now more of a pounding character. He had vomited occasionally during the past few days. On the day before admission he had such an attack in which he felt very faint, and there was apparently some clouding of consciousness associated with it. The family history revealed nothing relevant. The patient had had the usual diseases of childhood, including scarlet fever, but had always enjoyed a healthy active life. His history did not suggest urethral colic.

Examination.—There was a marked generalized arteriosclerosis. The superficial vessels were thickened and tortuous, especially the temporals and radials. Cardiac dulness was within normal limits, and there were no adventitious sounds. An electrocardiogram showed regular rhythm; normal A-V conduction; slurred QRS complexes, diphasic T wave in lead III and a ventricular rate of 90 per minute. The blood pressure was 240 systolic and 110 diastolic. The chest otherwise showed nothing pathologic. The abdomen was of scaphoid shape; there was no tenderness on palpation, and nothing pathologic was found.

There was some frequency of micturition; by day five or six times, by night two or three times. The urine showed nothing pathologic in several examinations. Urinalysis showed: specific gravity, 1.020; acid; no albumin; no sugar; no casts and no cells microscopically. The various tests of kidney function were not satisfactory on account of lack of cooperation by the patient. At one examination the urea content of the blood was slightly increased. The blood count showed: red cells, 4,000,000; white cells, 7,200; hemoglobin, 80 per cent. The Wassermann reaction of the blood was negative.

The ears, nose and pharynx were reported as not pathologic.

Mentally, though euphoric and exuberant, the patient was sensible.

The ocular fundi were normal and showed no evidence of any great amount of arteriosclerosis; there was no indentation of the veins where they were crossed by

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* Read at the Fifty-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 10, 1930.

the arteries. The fields of vision as determined by a rough test were not restricted. The pupils were equal and reacted to light and in accommodation. The right palpebral fissure was broader than the left; there was no limitation of any of the ocular movements, nor were they at any time associated with nystagmus. There was no weakness of any of the muscles of mastication. There was some flatness of the lower part of the right side of the face, giving the appearance of a relative lack of tone on the right side, so that when he smiled the right eye did not close as much as the left, and the nasolabial fold did not become so obvious on the right as on the left. At the same time there was no actual paresis on volitional movement.

He heard a watch at equal distances on the two sides. There was no trouble in swallowing; the palate elevated in the middle line. The tongue was protruded straight.

Muscular System: There was no atrophy of the muscles. The tone was relatively diminished in the left arm and leg. There was marked ataxia of the left arm and leg, especially toward the completion of the act of touching the nose and in the heel-to-knee test; this was of the characteristic cerebellar type, and was present with the eyes open or shut. There was no ataxia of the right arm or leg.

Fig. 1.—Diagram showing site of a lesion of the left superior cerebellar peduncle, involving the tractus spinothalamicus; made during life. *A* indicates the superior cerebellar peduncle; *B*, the tractus spinothalamicus; *C*, the mesial fillet; *D*, fifth nerve.

The rebound phenomenon was strongly positive in the left arm and leg. There was a relative diminution of power on the left side.

Sensory System: There was no loss of sense of position anywhere, and no astereognosis. There was a definite loss of pain and thermal sense over the whole right side, including the face.

Reflexes: All the tendon jerks of the arms and legs were present and not exaggerated. Neither the plantars nor the abdominals or epigastrics were obtained on either side. The organic reflexes were not affected.

Lumbar Puncture: Examination of the cerebrospinal fluid gave entirely normal results.

Gait: The patient walked on a broad base; especially was the left leg abducted, the left arm waving around like a flail all the time. The left leg was very uncertain in its movements. There was a subjective feeling of rotation from the left with the hands of the clock.

Diagnosis.—A diagnosis was made of a vascular lesion of the superior cerebellar peduncle involving the brachium conjunctivum and the tractus spinothalamicus on the left side outside the third nerve fibers (fig. 1).

Course.—The patient was discharged in July, 1929, to a home, but was readmitted on March 23, 1930, with bronchopneumonia. As far as the nervous system was concerned, the condition was as before except that he had in addition a left homonymous hemianopia.

Death occurred on March 29, 1930, from pneumonia.

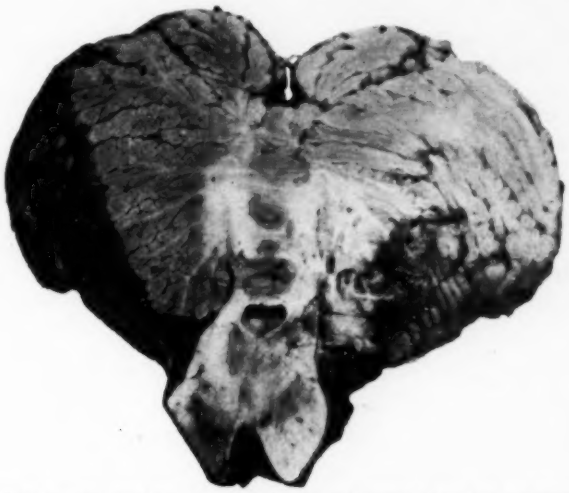

Fig. 2.—Horizontal section of cerebellum and pons showing an area of softening in the left cerebellar peduncle as diagnosed and extending on to the superior surface of the cerebellum.

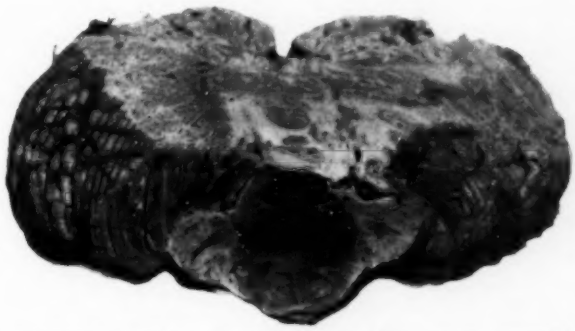

Fig. 3.—Transverse section of the pons to show more accurately the correspondence between the antemortem diagnosis and the actual lesion in the left superior cerebellar peduncle.

Autopsy.—Apart from the usual conditions in the lungs in pneumonia, a large stone was found blocking the first part of the right ureter, causing a great dilatation of the pelvis and an almost total degeneration of the kidney substance. It is remarkable that no history of pain had been obtained clinically, but this must have had at least an indirect influence in the causation of the raised blood pressure and marked generalized arteriosclerosis.

In the upper part of the pons, between the levels of the third and fifth nerves, there was on the left side a small area of softening which might have been made to order, just lateral to the fourth ventricle and involving the superior cerebellar peduncle with its brachium conjunctivum and extending ventrally sufficiently to involve the tractus spinothalamicus. This was due to a thrombosis of a branch of the superior cerebellar artery. It was entirely lateral to the fibers of the third nerve and above those of the fifth. This obviously accounted satisfactorily for the striking combination of symptoms—the ataxia on the homolateral side and the loss of pain and thermal sense on the heterolateral side (figs. 2 and 3). Such a combination of symptoms, in the absence of any involvement of the cranial nerves, could not be caused by a single lesion in any other situation.

While it is true that the softening extended superficially over a small area on the superior and anterior surface of the left cerebellum (fig. 3), and there must remain an element of doubt as to how much this added to the cerebellar symptoms, with the practically complete destruction of the fibers from the cerebellum to the red nucleus in the superior peduncle, it appears to me that this cerebellar extension of the lesion did not add any complicating factor.

COMMENT

When I showed the motion pictures illustrating this case, my attention was called to a fact which I had overlooked, that under the title "Hemianesthesia to Pain and Temperature, and Loss of Emotional Expression on the Right Side, with Ataxia of the Upper Limbs on the Left, the Symptoms Were Probably Due to a Lesion of the Thalamus or Superior Peduncle," [1] Dr. Charles K. Mills reported an almost identical case, the only difference being that in Dr. Mills' case, immediately after the onset, the cerebellar ataxia was confined to the upper extremity on the left side. There was no ataxia shown in the knee-to-heel test, and the gait was not affected. Also, his patient was deaf in the right ear. Apart from this, the loss of emotional expression on the opposite side of the face was even more marked than in my patient. During the four years this man was under Dr. Mills' observation, the ataxia of the left lower extremity developed.[2] Hence, the only points of difference remaining in the clinical observations were: 1. Deafness in the right ear. It is not stated whether this was of the middle ear or of the auditory nerve type. In my case examination by a specialist failed to reveal anything abnormal in the auditory apparatus. 2. The more intense loss of emotional expression on the right side of the face.

Low down and well anterior in my case, in the left internal capsule, there was another area of softening, which involved to a certain extent the anterior tip of the caudate nucleus (fig. 4). It was evidently too far forward to destroy the upper motor neuron fibers to the limbs, but I think that this may have accounted for the paresis in emotional move-

1. Mills, Charles K.: J. Nerv. & Ment. Dis. **35**:331, 1908.
2. Mills, Charles K.: J. Nerv. & Ment. Dis. **39**:73, 1912.

Fig. 4.—An area of softening well forward in the left internal capsule involving the caudate nucleus as the probable cause of the loss of emotional movements of the right side of the face with the full retention of volitional movements.

Fig. 5.—An area of softening in the area of the right posterior occipital artery accounted for the left homonymous hemianopia.

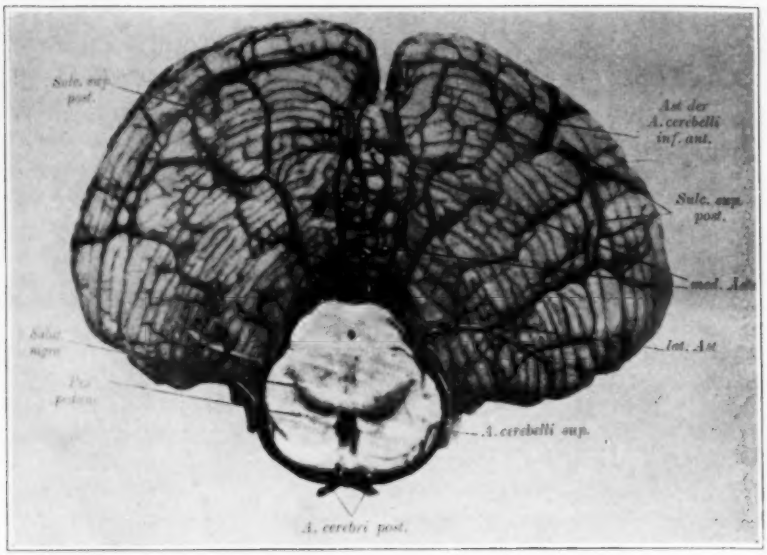

Fig. 6.—The distribution of the superior cerebellar artery. (After A. Jakob.)

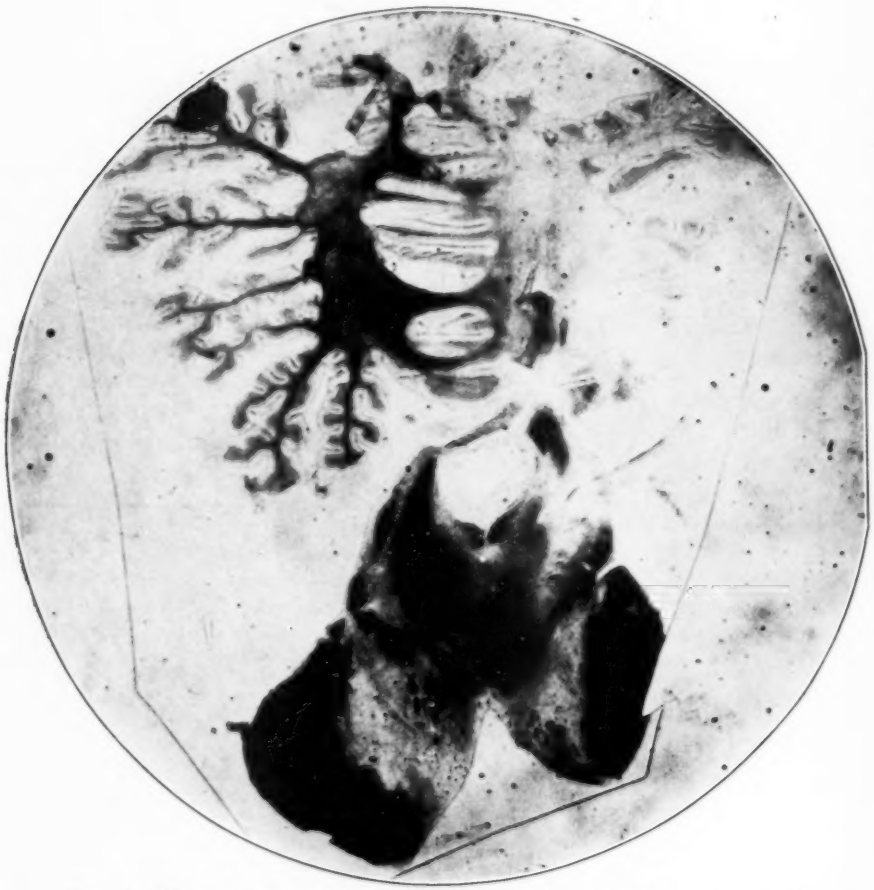

Fig. 7.—Weigert-Pal section showing degeneration in the brachium conjunctivum and tractus spinothalamicus on the left side.

ments on the right side. It certainly could not have been concerned in causing the syndrome I have described.

One frequently sees cases of hemiparesis that show a paresis of the face on volitional movement, but no asymmetry on emotional movement. I have several lantern slides to demonstrate this. To explain these I have surmised a lesion in the internal capsule above the level of the basal ganglia which interferes with volitional movement but not with the reflex arc with its receptive pathways through the auditory or optic chain to the basal ganglia, where I imagine the instincts and their emotional reactions must be seated. Dr. Mills' case and my own show the counterpart of this condition: loss of emotional expression, but no change of volitional expression. This is rather an extraordinary coincidence. Dr. William G. Spiller, who made the pathologic investigations in Mills' case—which unfortunately were never published, but which Dr. Spiller sent me—saw no macroscopic lesion in the caudate nucleus region, but in view of his observation that the lesion in his case was due to a syphilitic endarteritis, it is possible that multiple lesions may have existed.

A third lesion, which had evidently occurred between the first and last admission of the patient, had caused an area of softening in the distribution of the posterior cerebral artery and involved the occipital cortex and optic radiations on the right side (fig. 5).

SUMMARY

A case of thrombosis of the superior cerebellar artery is described, and a similar case is quoted from the literature; both cases show a definite combination of symptoms, namely, loss of pain and thermal sense on the homolateral side and ataxia, atonia and asthenia on the heterolateral side. Such a combination of symptoms could not be produced by a single lesion in any other place, and might well be named the syndrome of the brachium conjunctivum and the tractus spinothalamicus.

ABSTRACT OF DISCUSSION

Dr. William G. Spiller, Philadelphia: The case that Dr. Mills reported was almost identical, even to the sides that were affected. The man had no paralysis, but had extreme ataxia on the entire left side. He had no loss of tactile sensation on the right side, but he had loss of the sense of pain, heat and cold throughout the right side of the face and of the body. He had a complete unilateral loss of emotional movement of the right side of the face and there was no loss of voluntary movement of the seventh nerve.

I did the pathologic work for Dr. Mills. The lesion was an occlusion of the anterior cerebellar artery. The cerebellar cortex over the corpus dentatum was very much shriveled. The corpus dentatum on the left side was greatly degenerated; the left lateral fillet was practically destroyed, and the greater part of the brachium conjunctivum was destroyed.

There was one symptom in that case which has not been mentioned, the deafness in the right ear. The destruction of the left lateral fillet might explain the deafness of the right ear, but local causes were not ruled out.

Dr. Paul Schilder, New York: My attention was drawn to two features in this interesting picture. As far as my observation went, the patient halted before he reached his definite aim. This is an interesting contribution to the problem of bradyteleokinesis. It would conform to a case reported by Porot in which a lesion of the brachium conjunctivum provoked stopping of movements before the final aim was reached. It would indicate that the bradyteleokinesis is due to lesions of the brachia conjunctiva.

In the picture, another symptom attracted my attention. When the patient tried to reach his knee with his heel, he showed a marked degree of hyperflexion. I have found that this is a common symptom in cerebellar cases. It is not due to hypermetria in the sense of Babinski, but is based on a tendency to too strong an innervation of the flexors of the leg when there is a cerebellar lesion.

I should like to call attention to this hyperflexion in the lower extremities in cerebellar cases. It would be interesting to know in what way the patient reacted to turning of the head.

ENCEPHALITIC, IDIOPATHIC AND ARTERIOSCLEROTIC PARKINSONISM

A CLINICOPATHOLOGIC STUDY *

MOSES KESCHNER, M.D.
NEW YORK
AND
PAUL SLOANE, M.D.
PHILADELPHIA

The relatively small number of pathologic reports of cases of parkinsonism found in the literature as compared with the unusually large number of clinical reports, especially since the appearance of epidemic encephalitis in 1918, has prompted us to undertake this study. Our principal objects in this investigation were: (1) to put on record a number of additional cases of parkinsonism that have been observed clinically for a long period of years and finally subjected to detailed histologic study, and (2) to determine how far the clinical picture of parkinsonism can be correlated with the anatomic observations, especially as regards the site of the lesions.

Ten brains from cases diagnosed, during life, as parkinsonism were selected at random. In three of these the material had been in formaldehyde for years and took the various stains very poorly; this was particularly the case with the globus pallidus. Our report then consists of the anatomic observations in seven cases. Three of these were diagnosed, during life, as chronic encephalitic parkinsonism, two as idiopathic parkinsonism or genuine paralysis agitans and two as arteriosclerotic parkinsonism. In five cases, sections from the cerebral cortex, basal ganglia, hypothalamic region, mesencephalon, pons, medulla oblongata and cerebellum were examined; in the remaining two, which were cases from the older material, only the basal ganglia and mesencephalon were studied. In many instances serial sections were made. All sections were stained with cresyl violet, hematoxylin and eosin, van Gieson and Weil's modification of the Loyez method. Some of the sections were also stained with the Mallory, Victoria blue, Rio-Hortega, sudan III, Herxheimer and Perl stains.

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* Submitted for publication, May 20, 1930.

* From the Neurologic Wards and Laboratory of Neuropathology, Montefiore Hospital, New York.

REPORT OF CASES

CASE 1.—*Chronic Encephalitis. Parkinsonism.*

History.—A. Z., a woman, aged 37, was admitted to the Montefiore Hospital on Jan. 7, 1922, with the history that two years previously she had had an attack of influenza (?) that lasted for two weeks, during which she was drowsy and saw "double." Following this attack she remained well for one year, after which increasing weakness and rigidity of the entire body with attacks of excruciating pain in the head radiating to the spine gradually developed. Two months after admission a monotonous, quiet and slow speech developed.

Examination.—The patient was emaciated and presented typical parkinsonian facies and attitude; the right pupil was smaller than the left; both were irregular and reacted sluggishly to light and better in accommodation; facial innervation was poorer on the left; there was generalized muscular rigidity with "cog-wheel" phenomenon and loss of normal associated movements; there was a parkinsonian tremor of the head, tongue and all extremities; the deep reflexes were lively and the abdominal ones active; there were no pathologic reflexes. The speech was typically parkinsonian. No objective sensory disturbances were detected. The fundi were normal. The Wassermann reaction of the blood and cerebrospinal fluid was negative. The cerebrospinal fluid contained 11 lymphocytes per cubic millimeter; the colloidal gold curve was 0002343320. The urine was normal. The chemical analysis of the blood showed: urea (nitrogen), 15.3 mg.; uric acid, 1.7 mg., and blood sugar, 111 mg. per hundred cubic centimeters. The blood pressure was 140 systolic and 70 diastolic. The blood picture showed nothing unusual.

Course.—The condition gradually progressed; there appeared a "greasy face," "cog-wheel" movements of the extra-ocular muscles, more intense hypertonicity and marked atrophy of the deltoids and intrinsic muscles of the hands. Owing to the progressive general weakness and increasing helplessness, the patient became bedridden; the myocardium became feeble, the blood pressure dropped to 98 systolic and 70 diastolic, acrocyanosis appeared, and she died of pneumonia and cardiac failure seven years after the onset of the illness.

Necropsy.—There were: markedly contractured extremities, lobar pneumonia of the left lower lobe and a patent foramen ovale. The brain appeared smaller than normal, and the superficial vessels were deeply injected. Both middle cerebral arteries showed slight evidences of arteriosclerosis. The vessels of both thalami were markedly injected. The right pallidum and putamen were smaller than the left ones, and the right internal capsule was wider than the left. Both pallida appeared unusually pale and atrophic. The substantia nigra was also paler than normal.

Microscopic Examination.—There was a chronic leptomeningitis with marked increase and condensation of connective tissue in the pia-arachnoid.

The frontal lobes showed slight perivascular gliosis, scattered round cell infiltration (small lymphocytes and larger plasma cells) and an occasional degenerated ganglion cell, especially in the fifth layer of the cortex.

In the first and second pallidal layers, the number of large and small ganglion cells was apparently normal, but the former presented varying degrees of slight degeneration and neuronophagia. There was also some increase of glia nuclei (fig. 1). The number of the glia cells in the putamen was greatly increased, and many glia cell rests were present. There was moderate perivascular infiltration and neuronophagia with destruction of many large and small ganglion cells.

The ependymal lining of both thalami was normal. In all of the thalamic nuclei, including the pulvinar, there was slight perivascular infiltration of small round cells with increased glial reaction. The ganglion cells were well preserved.

In the subthalamic region the vegetative nuclei surrounding the third ventricle and the nucleus campi forelii showed severe degeneration of the ganglion cells varying in degree up to cell destruction and neuronophagia. There seemed to be

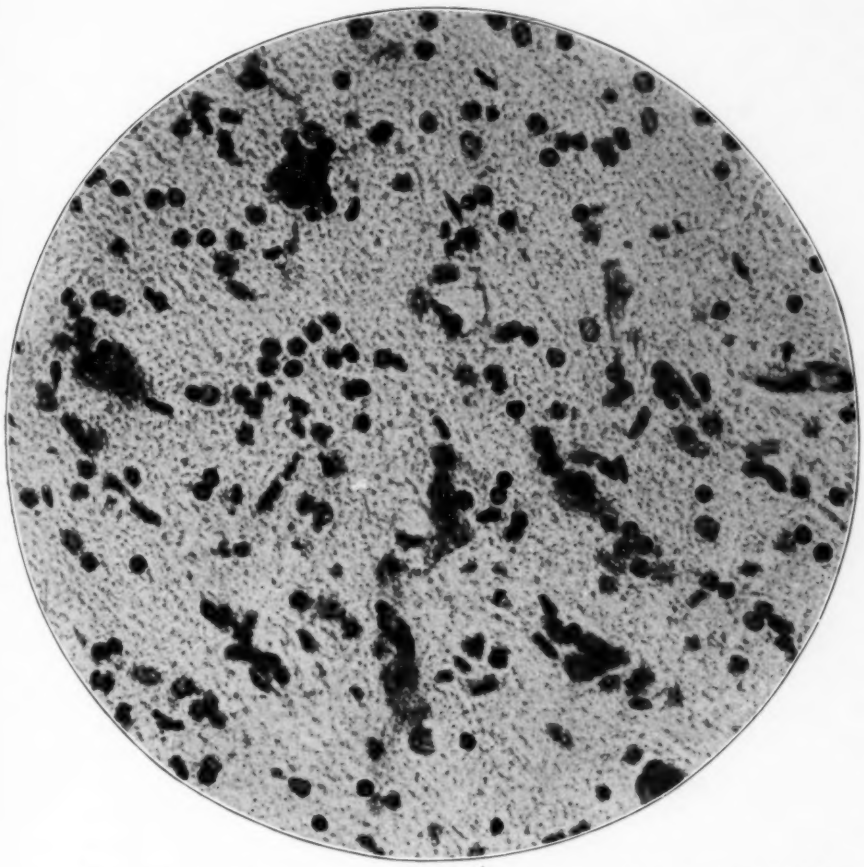

Fig. 1 (case 1).—Parkinsonism, chronic encephalitis. Globus pallidus showing cell destruction with varying degrees of neuronophagia and increase of glial nuclei. Cresyl violet stain.

an increase of subependymal glia toward the base of the brain. Perivascular infiltration was present throughout.

In the corpus luysii, a large number of ganglion cells appeared pale with the various stains. There was also a mild neuronophagia and moderate increase of glial nuclei.

Practically all of the pigmented cells of the substantia nigra showed pathologic changes; they were atrophied, with the pigment irregularly distributed throughout

the cell body. In the zona compacta most of the pigment cells had disappeared, those remaining being markedly swollen. Extracellular pigment was seen especially in the rostral portion, and numerous fine particles of pigment were scattered throughout the field. There was vascular congestion and marked perivascular infiltration with small lymphocytes. The field was densely packed with glia nuclei and nests of ganglion cells showing various degrees of neuronophagia. Pigment was also found in the perivascular lymph spaces.

The structures around the sylvian aqueduct seemed well preserved.

Slight neuronophagia with a marked increase in glia nuclei was present in the red nucleus, but no perivascular infiltration.

The pigmented cells in the locus caeruleus were fairly well preserved but there was an increase in the glia nuclei similar to that in the substantia nigra.

The inferior colliculi were conspicuous by the marked increase of glia nuclei and diffuse swelling of the ganglion cells with transitions to complete degeneration and neuronophagia. The changes in the superior colliculi were similar to those in the inferior, though not so marked.

Perivascular infiltration was present throughout the pons and the medulla oblongata, but there was no destruction of the nuclei.

Slight neuronophagia with marked increase in glia and intense perivascular infiltration were seen in the cornu ammonis.

No changes were observed in the cerebellum.

The Weil stain revealed a slight diminution of fibers in the neostriatum, but no changes in the pallidum. There was no demyelinization in the ansa lenticularis. Both sides of the anterior third of the lateral columns of the medulla appeared pale; under higher magnification this pale zone was found to be due to a marked diminution of the myelin sheaths. The fibers in the remaining two thirds of the lateral columns also showed degenerative changes, but these were less severe. Slight état criblé was seen in the pallidum, putamen, thalamus and substantia nigra.

The blood vessels did not show atheroma or calcification.

Comment.—The microscope revealed widespread inflammatory and degenerative lesions. Although the process was diffuse, involving the meninges, cortex, ependyma, pons, medulla and practically all of the basal ganglia, it seemed to have affected mostly the substantia nigra. Worthy of note is the fact that in a case of encephalitic parkinsonism of six years' duration no evidences of calcification were found in the brain. The isolated atrophy of the deltoids and intrinsic muscles of the hand may have been due to involvement of the anterior horn cells in the cervical cord (Wimmer's type of encephalitic amyotrophy); unfortunately, the cord could not be subjected to histologic investigation to confirm this hypothesis. The futility of attempting to correlate the clinical picture with the anatomic changes in a case of such diffuse pathologic involvement is obvious.

CASE 2.—*Chronic Encephalitis. Parkinsonism.*

History.—M. G., a married woman, aged 42, was admitted to the Montefiore Hospital on April 6, 1921, with the following history: About one year before, following great anxiety about her only son's illness and in the course of her last

pregnancy, an attack of "sleeping sickness" developed. During the first three days of the illness she was lethargic and delirious. Within the next few days she had recovered sufficiently to leave her bed; she remained well until after childbirth, following which she began to complain of marked general weakness and inability to do her housework. Two months later, she became unable to use the right upper and lower extremities, and noted a stiffness of the metacarpophalangeal joints of the right hand, with attacks of spasmodic contraction of the jaws and grinding of the teeth. During this period she had severe headaches and was extremely restless. Although she recognized the immediate members of her family, she lost all interest in life, became untidy, spoke very little and had to be watched continuously, lest she run away from her home.

Examination.—The pupils were irregular in contour and unequal in size, the left being larger than the right; both reacted sluggishly to light and better in accommodation. There were: poor convergence and bilateral ptosis; diminished ocular movements with "cog-wheel" phenomenon of the ocular muscles; a mask-like, greasy face with constant grimacing and drooling of saliva; generalized muscular rigidity, more marked on the right side; parkinsonian tremor of the head and right hand with a tendency toward catatonia; bilateral pyramidal tract signs with increased jerking of the jaw, patellar and ankle clonus and a positive Babinski sign, and emaciation with local atrophy of the thenar and interosseal muscles of the right hand. Mentally, she was sluggish in thought and speech, with marked poverty of emotional response, although the intellect, orientation and memory were unimpaired. All laboratory studies gave negative results. The blood pressure was 106 systolic and 64 diastolic.

Course.—The condition progressed rapidly. The patient became bedridden, and developed bedsores and severe nephritis with secondary anemia, succumbing to septicemia and bronchopneumonia about twenty-two months after the onset of the disease.

Necropsy.—There were penetrating decubitus ulcers, chronic nephritis and a marantic thrombus of the pulmonary artery. The brain weighed 1,220 Gm. and showed slight edema of the vertex. The gyri were unusually prominent, and the temporal lobe appeared to be flattened. The vessels and nerves at the base of the brain were normal. On section the brain and cord showed no gross abnormalities.

Microscopic Examination.—The frontal lobes, thalami, neostriatum, pons, medulla (nuclei) and cerebellum were normal.

The pallidum, red nucleus and corpus luysii showed only some slight perivascular infiltration.

The substantia nigra showed diffuse swelling of the ganglion cells, destruction of cells, considerable extracellular pigment (fig. 2) and marked increase in glia cells, but neither neuronophagia nor perivascular pigment. In some sections no remnant of a pigment cell was seen; the cells seemed to be entirely washed out.

With the cresyl violet stain the locus caeruleus showed a diminution in the number of cells and swelling and condensation of pigment in many of them. These changes were more marked in some areas than in others (fig. 4).

The ependyma was thickened in many areas and showed an increase of the subependymal glia. The ependymal cells were full of granules, particularly in the region of the aqueduct.

Changes in the fibers and état criblé were not seen.

The blood vessels showed slight thickening of the adventitia.

Comment.—The anatomic lesions in this case were degenerative and involved chiefly the substantia nigra and locus caeruleus. There were ependymal thickening, granulations, increase of subependymal glia and a slight adventitial thickening of the blood vessels. Except for the ependyma, the brain showed no evidences of glial proliferation. The pal-

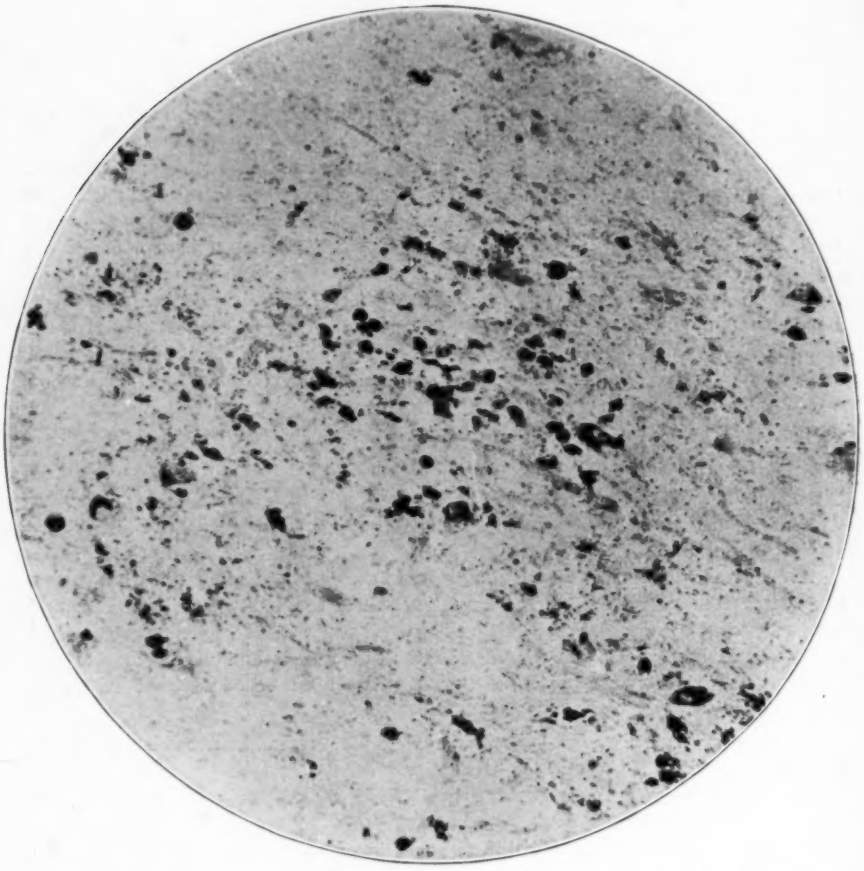

Fig. 2 (case 2).—Parkinsonism, chronic encephalitis. Section of the substantia nigra showing severe degeneration of the ganglion cells with much extracellular pigment. The number of ganglion cells is also markedly diminished. Cresyl violet stain.

lidum, corpus luysii and red nucleus showed perivascular infiltration; this, however, was so slight and out of proportion to what is usually observed in encephalitic parkinsonism, and the evidences of degeneration were so marked that histologically it was difficult to confirm the clinical diagnosis of chronic encephalitis. In this case also the brunt of

the pathologic process seems to have been in the substantia nigra, although the lesions in it were mostly degenerative. This case again illustrates the difficulty of attempting to correlate clinical signs with anatomic changes. The absence of lesions that would account for the

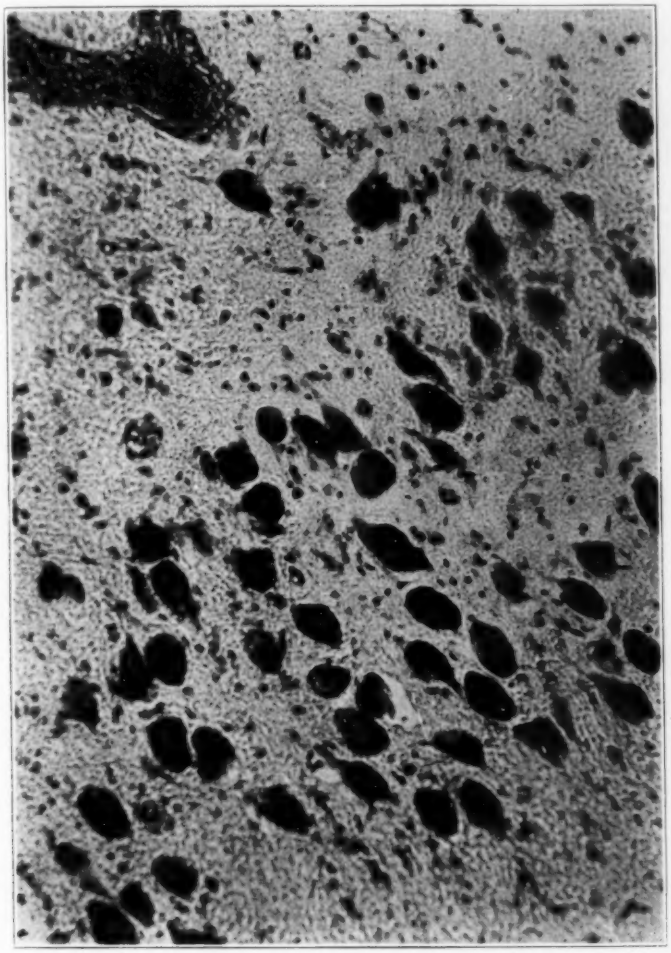

Fig. 3.—Section of normal locus caeruleus. Cresyl violet stain; reduced from × 220.

pyramidal tract signs, the involvement of the cranial nerves and the psychic changes are noteworthy, as is also the absence of lesions in the neostriatum that would account for the marked parkinsonian tremor.

Case 3.—*Chronic Encephalitis. Parkinsonism.*

History.—J. R., a married woman, aged 36, who was admitted to the Montefiore Hospital on Dec. 3, 1922, in 1919 had had an attack of influenza (?) during which

she suffered from dizziness, double vision, delirium and increased psychomotor activity with choreiform movements. Two days after the onset, she became lethargic, and remained so for four weeks. Apparently she recovered from this attack, and, except for vague pains in the hands and feet, she remained well until 1920, when tremor, bradykinesia and slow speech gradually developed. Her condition was then

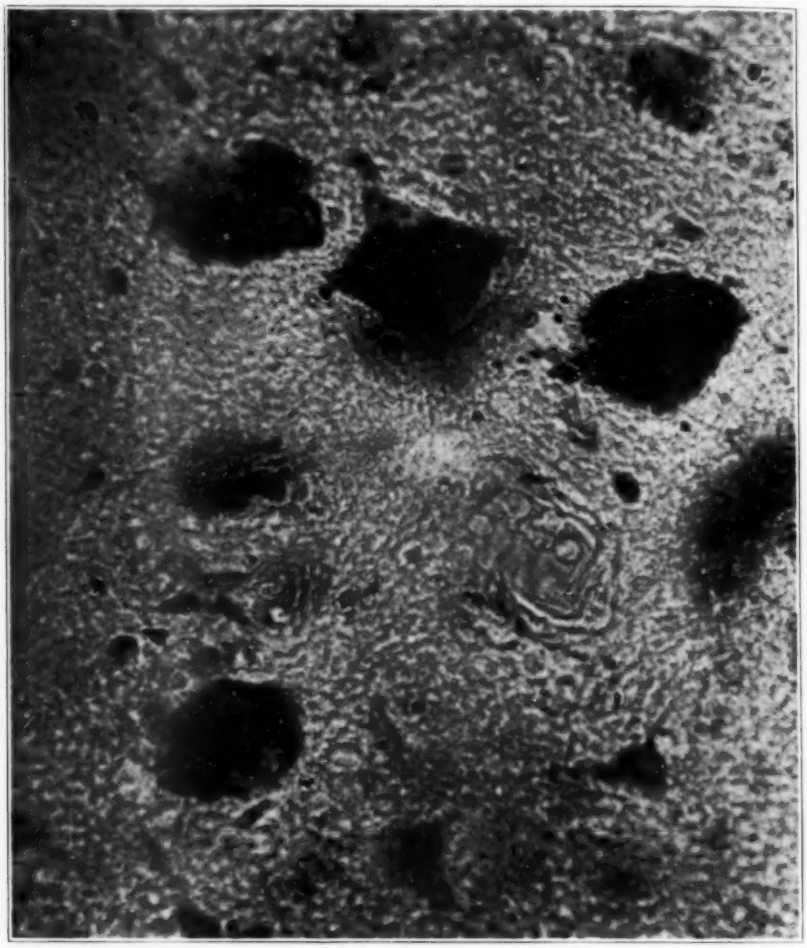

Fig. 4 (case 2).—Parkinsonism, chronic encephalitis. Section of locus caeruleus showing diminution in number of cells with swelling and condensation of pigment in some of the cells. Cresyl violet stain; reduced from × 440.

diagnosed as parkinsonism. One year later she became depressed, and made two unsuccessful suicidal attempts. In November, 1922, she became pregnant and aborted, and was curetted at the Fordham Hospital. Her recovery from the abortion was uneventful, and she was transferred to the Montefiore Hospital.

Examination.—There were: rigidity of all four limbs, with "cog-wheel" phenomenon; parkinsonian tremor; loss of normal associated movements; immobile facies; slow gait; right ptosis, and pupils sluggish to light and in accommodation. The tendon reflexes were hyperactive; the abdominal reflexes were active and equal; there was a bilateral Hoffmann sign but no Babinski sign. No objective sensory disturbances were discovered. The fundi were normal. All laboratory examinations gave negative results. The blood pressure was 130 systolic and 90 diastolic.

Course.—In January, 1923, the patient became euphoric and found difficulty in swallowing. She remained in this condition till July, 1923, when the rigidity became so marked that she appeared as if she were in partial "decerebrate rigidity," with the head in extreme hyperextension. She remained in bed during the next four years, merely vegetating, and in June, 1927, bronchopneumonia developed to which she succumbed seven years after the appearance of the parkinsonism.

Necropsy.—There were: markedly contractured extremities, emaciation, granular degeneration of all parenchymatous organs, pulmonary emphysema and terminal bronchopneumonia. The brain weighed 1,280 Gm. and showed slight edema of the meninges; the pia was opaque and thickened over the ventral surface of the pons and over the entire cerebellum, especially its dorsal surface. On section, the substantia nigra appeared paler on the right side than on the left.

Histologic Examination.—The meninges, cerebral cortex, cornu ammonis, external geniculate bodies, anterior corpora quadrigemina, pons, medulla (nuclei), hypothalamus, red nucleus, corpus luysii and cerebellum were normal.

The lateral nucleus of the thalamus showed some perivascular infiltration, but no marked glial reaction. The median nucleus was normal.

In the pallidum, the unusually darkly stained nuclei of the large and small ganglion cells were striking, as were the well differentiated glia nuclei with the cresyl violet stain. The nuclei of the small ganglion cells were unusually large, their average size being 8.3 microns as compared with 6.4 microns in sections from case 1; they were not granular, but appeared more homogeneous; under higher magnification these nuclei presented a fine, dustlike appearance. The large cells showed moderate early degenerative changes in the form of faint staining of the protoplasm. There was only a slight increase in glia, but no neuronophagia.

The changes in the putamen were similar to those in the pallidum. There was no evidence of perivascular infiltration in the striatum.

The caudal portion of the substantia nigra showed great diminution in the number of cells, those remaining being swollen and severely degenerated. There was a marked increase in glia nuclei (fig. 5).

The changes in the locus caeruleus were similar to those in the substantia nigra.

The globus pallidus showed slight état criblé.

The blood vessels showed no changes. There were no areas of calcification.

Comment.—Although the clinical history in this case was typical of encephalitic parkinsonism, there was little perivascular infiltration or glial reaction. The histologic picture was not that of a chronic encephalitic process, unless the unusually darkly stained large and small ganglion cells are to be interpreted as evidences of an inflammatory

process. It is noteworthy that neither this case nor case 1, both of which were of seven years' duration, showed calcareous deposits in or around the vessels in any of the sections examined.

This case also illustrates the futility of attempting to correlate clinical signs with anatomic changes. Although the lesions were diffuse,

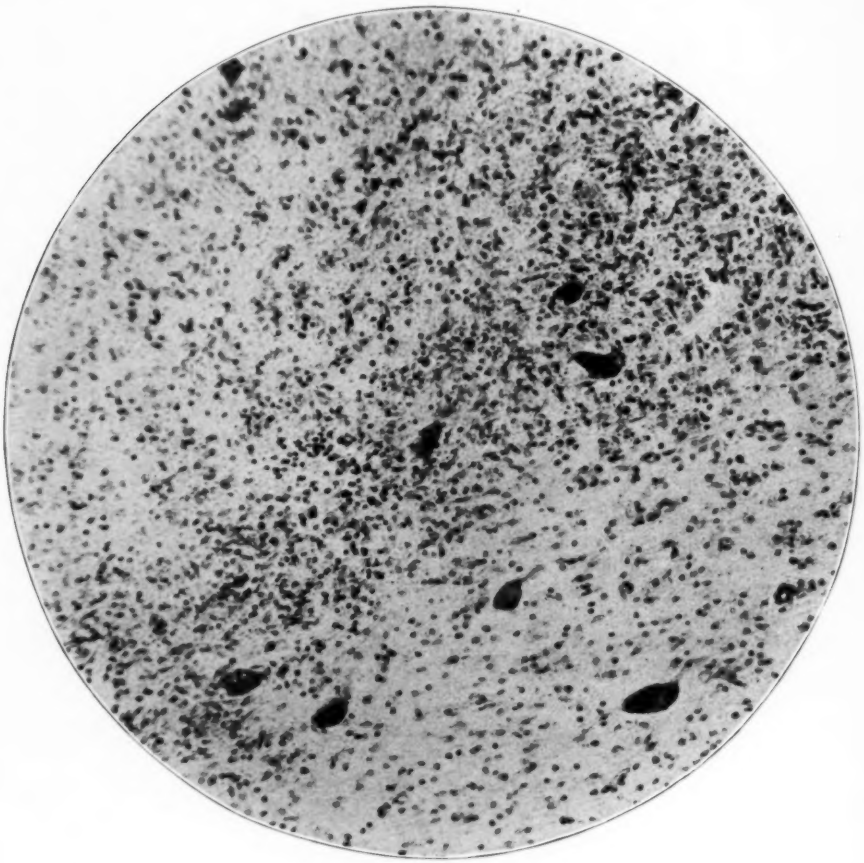

Fig. 5 (case 3).—Chronic encephalitic parkinsonism. Substantia nigra, showing diminution in number of ganglion cells with degenerative changes in the few cells remaining. Note the marked increase in glial nuclei. Cresyl violet stain.

they were not as extensive or as severe as those in case 1. The board-like decerebrate rigidity in this case, with no evidences of anatomic change in or around the red nucleus or its afferent or efferent tracts, with very little involvement of the substantia nigra, is noteworthy. Such marked rigidity in the absence of pallidal involvement is also noteworthy.

CASE 4.—*Paralysis Agitans (Idiopathic Parkinsonism).*

History.—E. S., a single woman, aged 55, was admitted to the Montefiore Hospital on April 7, 1927, with the history that in 1913 her left knee became stiff and painful so that she was unable to walk; at the same time she also became "nervous," and the left leg began to "shake." The case was diagnosed as neurasthenia and myositis; she was treated with massage without relief. In 1917, the right shoulder began to feel "tight" and "stiff;" gradually the other limbs became similarly involved, so that by 1922 the entire body became "stiff," and she "trembled all over."

Examination.—There were: typical parkinsonian facies, attitude and gait with fairly well preserved voluntary motor power; parkinsonian tremor of the head, tongue, fingers ("pill rolling") and toes; marked "cog-wheel" phenomenon in all joints; irregular but equal pupils, reacting well to light and in accommodation. All ocular movements were well performed, but there was some difficulty in convergence. There were a supranuclear (?) weakness on the left side of the face, positive Hoffmann and Babinski signs and diminished abdominal reflexes on the left side. The medical examination and all laboratory studies gave negative results. The blood pressure was 112 systolic and 72 diastolic.

Course.—After admission to the hospital, the condition progressed rapidly. Owing to contraction of the muscles of the neck, swallowing became progressively more difficult, and the patient died of inanition and exhaustion on June 6, 1927, fourteen years after the onset of the illness.

Necropsy.—There were: marked arteriosclerosis of the aorta and brown atrophy of the parenchymatous organs. On gross section the brain showed état criblé and état marbré in both corpora striata.

Histologic Examination.—The cortex (frontal and occipital poles, prerolandic and postrolandic areas), locus caeruleus, periaqueductal structures, pons, medulla, cornu ammonis, cerebellum and meninges were normal. The blood vessels throughout the brain did not show marked arteriosclerotic changes or perivascular infiltration suggestive of an inflammatory process.

The small ganglion cells of the pallidum appeared fairly well preserved, but the large ganglion cells were practically destroyed; in sections stained by the Weil method a pronounced état marbré was observed.

In the neostriatum scarcely a normal large ganglion cell was seen; most of them were swollen, with their nuclei displaced toward the periphery; in others, the cytoplasm took the stain very faintly, and presented a honeycomb appearance. The walls of the cells were lined by a thin layer of darkly stained substance (cresyl violet). The small ganglion cells showed no marked changes. No glial reaction or neuronophagia was seen. The right putamen showed marked cystic degeneration with scattered small round cells and gitter cells.

Throughout the thalamus there were chronic degenerative changes in the ganglion cells, as evidenced by the irregular outline and displacement of the nuclei, distortion of the cell body, diffuse discoloration of the cytoplasm and accumulations of densely stained masses at the periphery. In some areas only shadows of cells were left. There was no evidence of glial reaction. No noteworthy changes were seen in the corpus luysii.

There was diffuse swelling of the pigment cells with scattered destruction and depigmentation in the substantia nigra. The destructive process, however, was not as marked as in the encephalitic cases, nor was the glial proliferation as pronounced.

The ganglion cells were diminished in number in the locus caeruleus. The great majority of those remaining showed marked degrees of swelling with loss of pigment. Some of the cells were almost completely destroyed (fig. 6).

The ganglion cells of the red nucleus were swollen, and contained an increase of lipochrome. Many of them had begun to undergo destruction and showed varying degrees of neuronophagia (fig. 7).

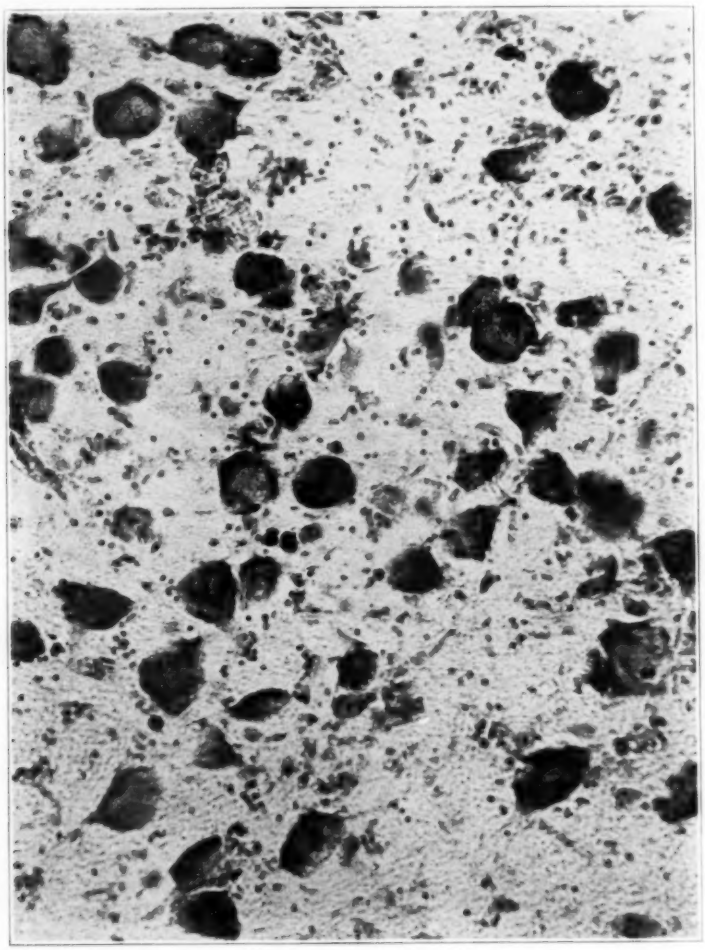

Fig. 6 (case 4).—Idiopathic parkinsonism. Locus caeruleus showing marked degree of swelling of ganglion cells with loss of pigment. There is some diminution in the number of cells. Some of the cells have undergone almost complete destruction. Compare with figure 3. Cresyl violet stain; × 220.

The lower third of the striopallidal fibers showed état criblé and état marbré, the upper two-thirds being normal. Some état criblé was also seen in the pallidum, putamen and within and around the red nucleus.

The blood vessels showed no changes.

Comment.—The lesions of idiopathic parkinsonism in this case were found in the neostriatum, pallidum, thalamus, red nucleus, substantia nigra, locus caeruleus and the lower third of the striopallidal fibers. The lesions were bilateral and more or less symmetrical. The severest lesion

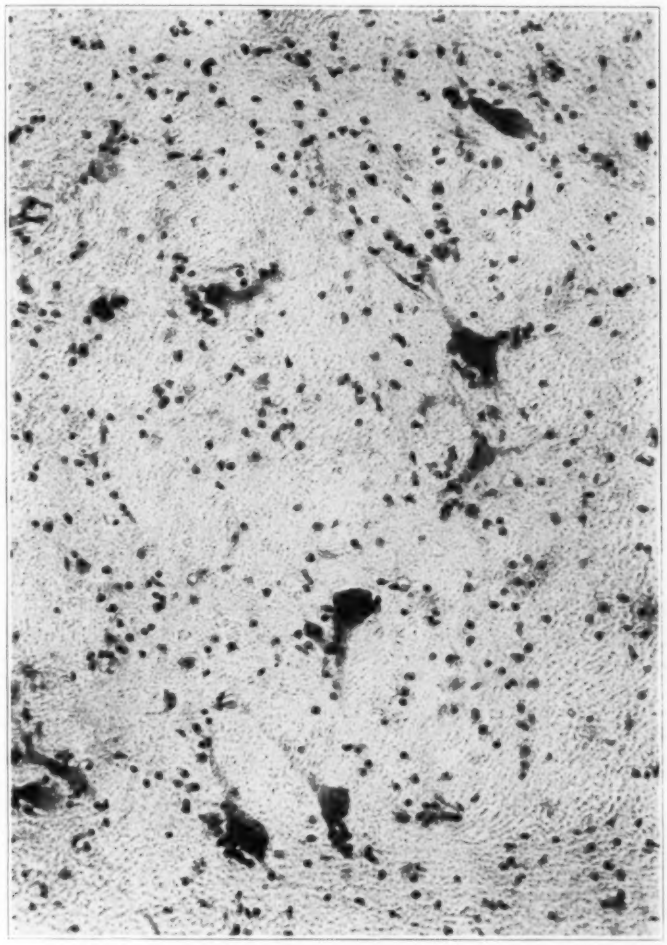

Fig. 7 (case 4).—Idiopathic parkinsonism. Section of red nucleus showing swelling and destruction of ganglion cells with varying degrees of neuronophagia. Cresyl violet stain; reduced from × 220.

was found in the right putamen, which had been entirely destroyed by cystic degeneration. The substantia nigra was least involved. The lesions were predominatingly of chronic degenerative nature with état criblé and état marbré, with no perivascular infiltration and only a slight amount of glial proliferation. It is noteworthy that in both the pallidum

and the neostriatum the large ganglion cells seemed to have been mostly involved in the degenerative process. The vessels showed no changes, the entire process being one of cell destruction—a primary degeneration. The complete destruction of the right putamen may possibly be interpreted as evidence that this structure was the first to be

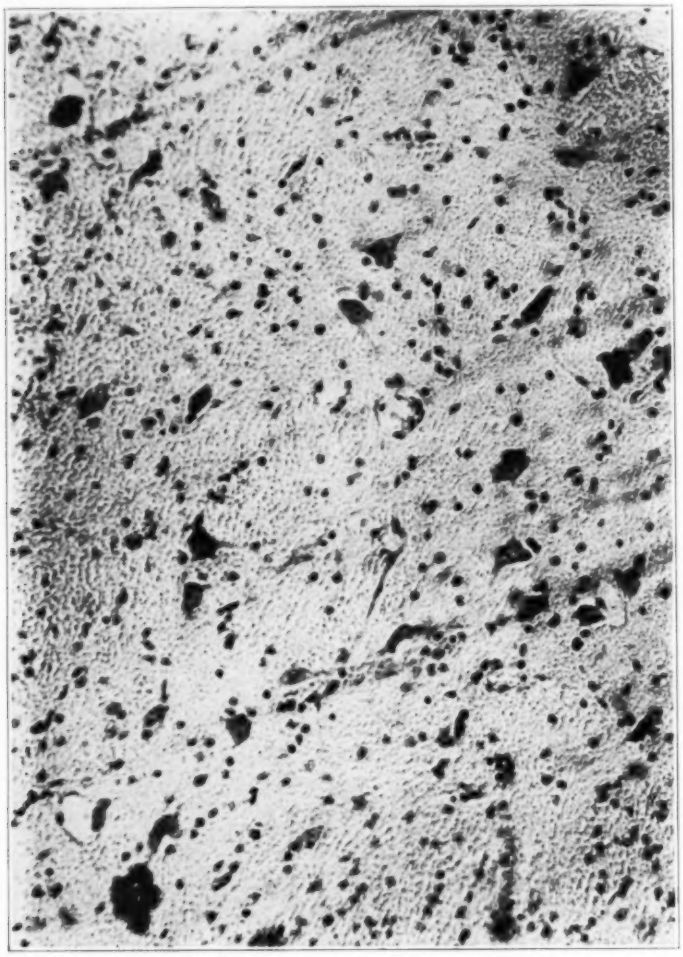

Fig. 8.—Section of normal globus pallidus. Cresyl violet stain; reduced from × 220.

affected by the disease, and therefore may account for the earliest sign of the disease, the marked tremor in the left side of the body. The lesions in the thalamus are probably sufficient to account for the severe pain that the patient experienced at the onset of the disease. In this case there were again no anatomic changes to account for the mild though definite pyramidal tract signs on the left side of the body.

CASE 5.—*Paralysis Agitans (Idiopathic Parkinsonism).*

History.—G. S., single, a seamstress, aged 50, was admitted to the Montefiore Hospital on March 6, 1914, with the following history: In 1911, one year after the death of both of her parents within two months, she noticed a shaking of the middle finger of the right hand, which soon involved the remaining fingers. A few months later, the right foot began to shake; this was followed by a trembling of the left upper and finally of the left lower extremity. She kept on working, however, until 1913, when, owing to a beginning "stiffness" in the joints and an "accelerating" gait, locomotion became impaired. She had always been constipated. The menses had begun at 17, were regular and ceased uneventfully at 49. For some years she had been suffering from a ravenous appetite, excessive thirst, frequent urination and pruritus vulvae. This condition was diagnosed as diabetes mellitus, and treated accordingly. (Further information as to blood sugar, etc., could not be obtained.) Some months before admission to the hospital, pains in the legs and paresthesias in the hands also developed.

Examination.—There were: a typical parkinsonian facies, attitude, gait and speech, with parkinsonian tremor and rigidity and "cog-wheel" phenomenon in all large joints and contractures of the fingers and toes. Except for somewhat diminished tendon reflexes, the neurologic examination gave negative results. There were also evidences of a moderate sclerosis of the peripheral blood vessels, a large fibroid tumor of the uterus and a chronic vulvovaginitis. The urine contained 4.5 per cent of sugar, and there was a moderate hyperglycemia. Roentgen examination revealed chronic arthritic changes in all small joints. All other laboratory examinations gave negative results. There was no hypertension. There were no psychic disturbances.

Course.—The parkinsonism gradually progressed, and the patient became bedridden. Two months before death, multiple skin abscesses, septicemia, acetonuria and diabetic coma developed, to which she succumbed on Sept. 8, 1917, six years after the onset of the illness.

Necropsy.—There were: multiple superficial and deep abscesses, healed pulmonary tuberculosis and fatty degeneration of the islands of Langerhans. Except for occasional thickening of the cerebral vessels, macroscopic examination of the brain gave negative results.

Histologic Examination.—(Only the midbrain and basal ganglia were studied.) In the pallidum, putamen and caudate nucleus the small ganglion cells took the cresyl violet stain very poorly; they appeared shrunken and distorted and their nuclei were displaced toward the periphery.

The ganglion cells of the thalamus seemed to be fairly well preserved, except that here and there the nuclei were displaced and appeared swollen.

In the corpus luysii and red nucleus changes similar to those in the thalamus were noted.

In the substantia nigra the cells were diminished in number, swollen and broken down, and contained very little pigment, most of the latter being within the perivascular spaces. There was no glial proliferation, but glia cells containing pigment were found in and around the blood vessels. There were very few normal ganglion cells remaining, and some of these showed vacuolization.

The locus caeruleus presented a picture similar to that of the substantia nigra.

Comment.—In this case the lesions were purely degenerative, with apparently the severest involvement in the substantia nigra and less involvement in the other basal ganglia. The severe involvement of the

substantia nigra in this case was in marked contrast to the slight involvement in case 4, which was also diagnosed clinically as idiopathic parkinsonism. The involvement of this structure was as marked as in the cases of encephalitic parkinsonism. The relatively slight glial proliferation and very slight état criblé in the pallidum in this case, in contrast to the other idiopathic case (case 4), is noteworthy. From the severity of the clinical manifestations of parkinsonism in this case, one expected a much more intense pathologic process than was actually found. Whether or not the diabetes was responsible for this disparity between the clinical features and the pathologic changes, we cannot state. We also wish to point out that in this case, in which there was marked rigidity and tremor, the only cellular involvement in the striatum and pallidum was a moderate degeneration of the small ganglion cells, the large ganglion cells remaining intact.

CASE 6.—*Arteriosclerotic Parkinsonism.*

History.—M. F., a housewife, aged 50, was admitted to the Montefiore Hospital on July 10, 1926, complaining of increasing constipation, urinary incontinence and dysuria for two years, and dyspnea, precordial pain, generalized shooting pains and a sensation of "burning" and of "pins and needles" in the back and in the upper and lower extremities for one year. All of these symptoms were attributed to grief following the death of an only son, one year before the onset of the illness. As time went on she noticed a progressive weakness and stiffness in the neck and in all limbs. Locomotion, at first difficult, soon became impossible. Except for rheumatic (?) pains in the joints since childhood, the previous history was of no significance.

Examination.—There were: a fixed facies, generalized muscular rigidity with a "cog-wheel" phenomenon, more marked in the left upper and lower extremities, loss of automatic and normal associated movements, exaggerated tendon reflexes, more marked on the left side, positive Babinski and Hoffmann signs on the right side and absent abdominal reflexes on both sides. There was no tremor. Memory was poor for recent and past events, and there was marked lack of attention and mental concentration. The fundi were markedly arteriosclerotic, and there was also a moderate sclerosis of the peripheral vessels, with accentuation of the second aortic sound. The blood pressure was 124 systolic and 80 diastolic. The Wassermann reaction of the blood and spinal fluid was negative. Urinalysis revealed a specific gravity of 1.020; the urine was full of albumin and hyaline and granular casts. Examination of the blood showed: hemoglobin, 82 per cent; red cells, 4,800,000; white cells, 5,000; no abnormal cells; urea nitrogen, 13.3 mg., and sugar, 104 mg. per hundred cubic centimeters.

Course.—Within a few weeks after admission, the condition became progressively worse, the dyspnea more intense and the circulation more embarrassed. The patient died of uremia on Oct. 18, 1926, one year after the onset of the illness.

Necropsy.—There were: cardiac dilatation on the right side, pulmonary congestion, arteriosclerotic kidneys, hyalonephrosis, hemorrhagic cystitis, healed bilateral pulmonary tuberculosis with bronchiectatic dilatations, brown atrophy of the liver and moderate general arteriosclerosis. On gross examination, the brain appeared normal, except for mild arteriosclerosis of the vessels at the base.

Histologic Examination.—The first and second pallidal layers showed marked gliosis. The large ganglion cells were fairly well preserved, but some of them showed varying degrees of swelling and atrophy and presented a dustlike appearance with poor staining qualities. There was a reduction in the number of large cells (fig. 9). However, the destructive changes in the cells were much less

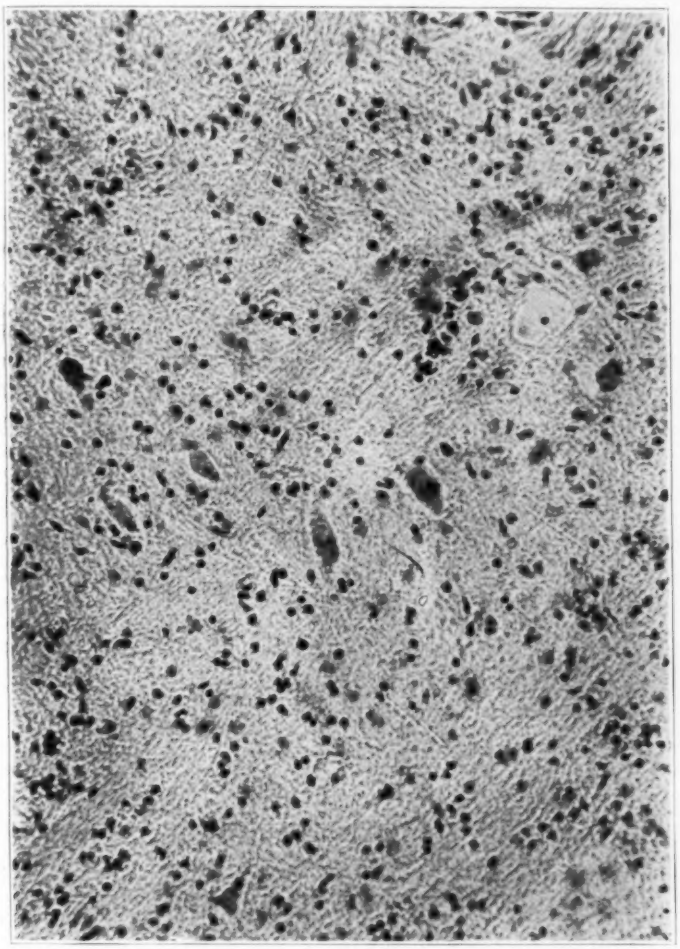

Fig. 9 (case 6).—Parkinsonism, cerebral arteriosclerosis. Section of globus pallidus, showing increased number of glial nuclei, with some reduction in the number of large ganglion cells and the poor staining qualities of those present. Compare with figure 8. Cresyl violet stain; reduced from × 220.

marked than the gliosis. With the sudan III stain most of the large ganglion cells were seen to be filled with coarsely granular orange masses, while the small ganglion cells showed stippling with fine orange granules.

The nuclei of most of the large ganglion cells of the neostriatum were irregular in outline and eccentrically situated, and were surrounded by an accumulation

of a darkly stained substance. The cell bodies themselves were also irregular in contour and devoid of Nissl bodies. In contrast to the severe changes in the large ganglion cells, the small ganglion cells showed much less involvement; they were diminished in number, and there was a marked increase in glia nuclei with scattered neuronophagia. The thalamus showed only some slight increase in the number of glia cells and neuronophagia. The hypothalamus was normal, except for the presence of subependymal glial reaction.

Most ganglion cells in the red nucleus were distorted and diffusely swollen, the remaining ones being destroyed. The cytoplasm was darkly stained and indicated a chronic process. Various stages of neuronophagia and mild gliosis were also present. In contrast to the idiopathic cases, the red nucleus showed much more involvement in this case.

In the cephalic portion of the substantia nigra there was abundant proliferation of glia with marked destruction of the cells and much extracellular pigment. The process had apparently been arrested, and the pigment débris had already been removed. A more caudal section showed practically no changes.

The changes in the locus caeruleus were similar to those in the substantia nigra.

The striopallidal fibers did not show demyelinization. With the Weil stain whole vertical sections of the brain (rolandic area) showed a distinct pallor in the left corona radiata and internal capsule, but there was no descending degeneration of the pyramidal tracts in the pons and medulla.

Marked état criblé, especially in the pallidum and putamen, as well as in the thalamus, internal capsule and corona radiata, was seen (fig. 10).

The cortex (frontal, occipital and prerolandic regions), pons, cerebellum and cornu ammonis were normal.

The meninges were edematous and contained within their meshes scattered areas of round and granular cells as well as extravasations of red cells, but no perivascular infiltration.

There were numerous plaques of perivascular edema distributed all over the brain, with thickening of the glial margin (état precribatus). In the basal ganglia the arteries showed thickening, especially of the intima and media, with the formation of connective tissue in the latter and a well preserved lamina elastica. The smaller vessels frequently showed advanced hyaline degeneration. In addition to these changes, there were also evidences of perivascular infiltration with gitter cells.

Comment.—In this case of arteriosclerotic parkinsonism the predominating lesions were a diffuse, marked increase in glia nuclei, status cribratus, degeneration of ganglion cells and scattered neuronophagia in the basal ganglia. The process was apparently chronic, and was associated with perivascular infiltration with gitter cells, especially in the pallidum. The red nucleus showed much severer involvement in this case than in the encephalitic and idiopathic cases. The arteries at the base of the brain and in the basal ganglia showed thickening of the intima and media, with formation of connective tissue in the latter. Although there was some evidence of degeneration in the left corona radiata and internal capsule, the cortex showed no lesions that could be attributed to an acute apoplectiform insult or to an incomplete vascular occlusion, unless the numerous plaques of perivascular

edema distributed all over the brain with thickening of the glial margin could be interpreted as evidences of poor nutrition of these parts of the brain owing to diseased vessels.

The anatomic observations can hardly be correlated with the clinical picture. The entire process was apparently much more chronic than could be expected in a case of only one year's duration. So far as the site of the lesions was concerned, there was very little difference between this case and the encephalitic cases.

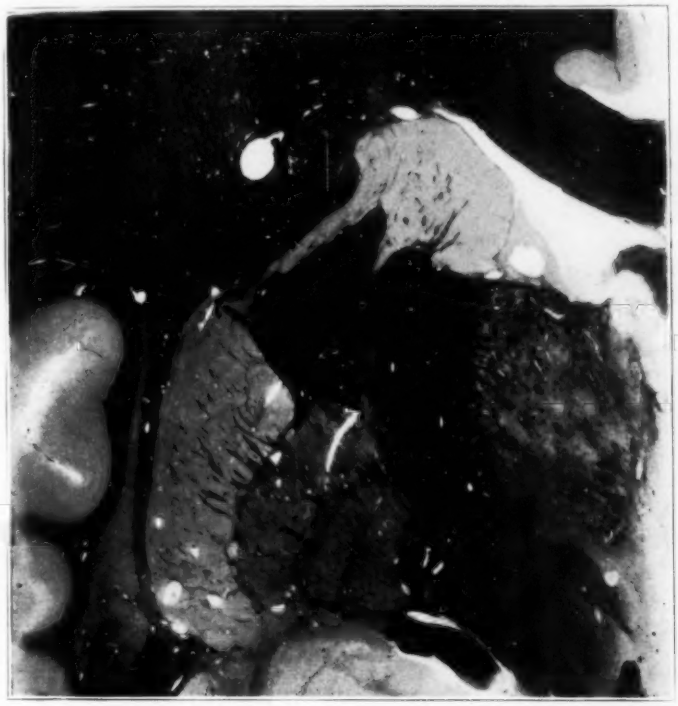

Fig. 10 (case 6).—Parkinsonism, cerebral arteriosclerosis. Section showing areas of demyelinization in the striatum, thalamus and corona radiata. Weil stain.

CASE 7.—*Arteriosclerotic Rigidity (Parkinsonism).*

History.—B. F., a man, aged 57, was admitted to the Montefiore Hospital on April 19, 1926, complaining of weakness in both legs and difficulty in walking for five years, a slowing of all volitional movements, including speech, and impaired memory for two years. For years he had had nocturia, cardiac palpitation, dyspnea on exertion, hypertension and periodic attacks of excruciating headache and pain in the back. He had always been constipated. Three months before admission his weight was 220 pounds (99.7 Kg.). He was not alcoholic, nor was he exposed to chronic metallic poisoning. He said that he had not had venereal infection.

Examination.—There were: marked sclerosis of the peripheral vessels, pulmonary emphysema and cardiac hypertrophy with dilatation. Neurologically, there were evidences of pseudobulbar palsy (bilateral Babinski and Hoffmann signs, markedly exaggerated deep reflexes, muscular hypertonicity, "marche à petits pas," etc.) and arteriosclerotic fundi. There was no tremor. Although he was extremely sluggish mentally, memory and judgment seemed unimpaired. Speech was thick and retarded. The Wassermann reaction of the blood and cerebrospinal fluid was negative. Urinalysis showed: specific gravity, varying between 1.025 and 1.040, and a large amount of albumin, with granular, epithelial and hyaline casts and numerous red blood cells. There was 14 mg. of urea nitrogen per hundred cubic centimeters of blood. The blood pressure was 206 systolic and 128 diastolic. The diagnosis was essential hypertension with multiple cerebrovascular insults.

Course.—The patient was put to bed and treated for the cardiovascular-renal condition. On Oct. 22, 1926, he was discharged as "somewhat improved," so far as the medical condition was concerned; neurologically he was in statu quo.

He was readmitted to the hospital on July 6, 1927, when a medical examination revealed practically the same conditions as on the first admission. Neurologically, he presented a pseudobulbar syndrome with markedly diminished voluntary motor power and intense muscular rigidity. The left pupil was larger than the right and did not react to light. There were: bilateral supranuclear facial weakness; inability to protrude the tongue; weakness of the soft palate; hyperreflexia of all tendon reflexes with bilateral ankle clonus; the abdominal and cremasteric reflexes were absent, with positive Hoffmann and Babinski signs on the left side; weakness of the left motor trigeminus; left hemihypalgesia; no tremor and no "cog-wheel" phenomenon. The speech was bulbar; the patient was unstable emotionally. The fundi were atherosclerotic. The condition remained practically unchanged until death from cardiac decompensation, general weakness and exhaustion on Sept. 10, 1927.

The neurologic diagnosis was pseudobulbar palsy and arteriosclerotic parkinsonism.

Necropsy was limited to the brain. Except for marked thickening of the cerebral vessels, gross examination of the brain and meninges gave negative results. No hemorrhages were seen.

Histologic Examination.—Only the midbrain, basal ganglia and blood vessels were studied in detail. Sections through the middle cerebral artery showed marked thickening and proliferation of the endothelial layer; the adventitia was not thickened, but showed scattered areas of round cell infiltration. Similar changes were found in the arteries of the pons and medulla. Occasionally, hyalinization of the smaller vessels was seen, and several vessels were filled with organized thrombi. An especially marked arteriosclerotic vessel was found in the right putamen.

In the first pallidal layer most of the ganglion cells had disappeared, and those remaining were shrunken and showed eccentrically displaced nuclei. There was no perivascular infiltration and no glial proliferation. Some neuronophagia was present. All cells took the various stains very poorly. No changes were observed in the second pallidal layer. The ganglion and glia cells of the neostriatum showed an abundance of finely granular dark pigment. No changes were observed in the claustrum.

The ganglion cells of the thalamus showed marked swelling. There were several minute areas of softening; these were apparently of recent onset, since gitter cells were still present.

The red nucleus, corpus luysii and substantia nigra showed only marked sclerosis of the blood vessels.

The ependyma was markedly thickened, and many of its vessels showed arteriosclerotic changes.

État criblé was seen in the neostriatum and thalamus, but was especially marked in the pallidum; the right internal capsule showed a pale zone with many arteriosclerotic vessels surrounded by areas of demyelinization (fig. 11).

Comment.—The noteworthy anatomic observations in this case were: marked arteriosclerosis of the medium and small cerebral

Fig. 11 (case 7).—Parkinsonism, cerebral arteriosclerosis. Section showing areas of demyelinization in the striatum, thalamus and internal capsule.

vessels; thickened ependyma; severe degeneration of the ganglion cells with some slight neuronophagia in the first pallidal layer, neostriatum and thalamus; areas of demyelinization in the right internal capsule surrounding the arteriosclerotic vessels. Many of the vessels were filled with organized thrombi, but there were no softenings and no hemorrhages in any of the sections that were examined. Except for arteriosclerotic vessels, the red nucleus, corpus luysii and substantia nigra were apparently free from changes. Worthy of comment in this case is the absence of tremor in the presence

of severe lesions in the putamen. It is also noteworthy that although the akinesia and hypertonicity were as marked as in any of our cases of encephalitic or idiopathic parkinsonism, the severity of the lesions in the pallidum, red nucleus, corpus luysii and substantia nigra in this case was nothing like that observed in the other cases. The case also illustrates the futility of attempting to correlate the clinical manifestations of a disease with the anatomic changes when they are as diffuse as they usually are in cases of cerebral arteriosclerosis.

COMMENT

Chronic parkinsonism at times presents unusual difficulties in determining clinically whether it is due to encephalitis (epidemic), to genuine or so-called idiopathic paralysis agitans or to cerebral arteriosclerosis. The difficulty is especially great in persons who have reached an age at which cerebral arteriosclerosis may be expected, and who, in addition, give a history of an infection of the upper respiratory tract or grip preceding the onset of the parkinsonian syndrome.

The literature contains descriptions of various criteria that may be helpful in this differentiation. Hall [1] mentioned the following characteristics of parkinsonism due to encephalitis: typical "pill-rolling" tremor is absent or minimal; tremor may be absent no matter how general the rigidity is; whereas in so-called idiopathic paralysis agitans it is not unusual for one extremity or one side of the body to be affected at first and, as a rule, for the condition to extend fairly soon; in encephalitic cases, as the years go on such extension does not occur; muscular jerkings, lethargy, pupillary signs, great restlessness, spasmodic fixation of the jaws, nystagmus and disturbances in ocular convergence are more common than in the idiopathic cases; the fixed facies develops much more slowly and later in the encephalitic than in the idiopathic cases; in encephalitic cases the parkinsonian syndrome may remain stationary and even improve; such is never the case in the idiopathic type.

From our own observation we may add that the encephalitic type is characterized by a fairly acute onset of the symptoms and signs of parkinsonism—within two or three days after the acute onset of the encephalitis. In acute parkinsonism the symptoms may disappear as the acute symptoms of the encephalitis subside, but more often there is a tendency to progression; this tendency, however, is greater in cases in which the parkinsonism appears late in the disease or as a relapse after apparent recovery. The period of apparent well-being between the sub-

1. Hall, A. J.: Encephalitis Lethargica, Lancet **1**:731 (April 14) 1923.

sidence of the acute symptoms and the onset of the parkinsonism may vary from a few days to one or more years. This interval is usually longest in cases of subacute or chronic encephalitis. The usual history obtained from these patients is that an attack of epidemic encephalitis occurred with gradual recovery, after which the parkinsonian syndrome developed and the patient entered a stage during which he may or may not have been lethargic.

Generally speaking, the tremor in the encephalitic cases is coarser, less constant and less marked; sometimes it is overshadowed by the massive muscular rigidity, giving rise to "paralysis agitans sine tremore." When present, the tremor may often be associated with ataxia resembling that of multiple sclerosis, a phenomenon never observed in the tremor of genuine paralysis agitans.

The association of the parkinsonian syndrome with symptoms and signs referable to involvement of the pyramidal tracts and bulbar nuclei (myasthenia) is common in encephalitis and never observed in uncomplicated genuine paralysis agitans.

Symptoms due to disturbances of the vegetative nervous system, such as the "greasy face" and diabetes insipidus, are not so frequent nor so marked in idiopathic as in encephalitic cases. Choreiform, myoclonic, ticlike and dystonic movements, as well as a tendency to catatonia, in association with the characteristic parkinsonian tremor and hypertonicity, so common in the encephalitic cases, are never observed in the idiopathic form. The same may be said of oculogyric and cephalogyric crises.

Another diagnostic feature of encephalitic parkinsonism is a diurnal variation in the patients' motor activities. Sleep disturbances in the nature of a "reversal of sleep" and various disorders of breathing, such as grunting hyperpnea, dyspnea, ptarmus and all sorts of respiratory tics, are also never observed in genuine paralysis agitans.

In contrast to the cases of idiopathic parkinsonism, in patients with encephalitic parkinsonism there is a strong tendency for various psychic disorders to develop; these are most common in younger persons, especially in children, and are characterized by a complete change in personality. Disobedience, excessive irritability, unprovoked fits of temper, cruelty, destructiveness, lying and various psychosexual abnormalities have been observed. An important feature of the psychic disorder in these persons is that the change in personality is seldom accompanied by a corresponding degree of intellectual impairment.

A complete or partial parkinsonian syndrome is often observed in persons suffering from cerebral arteriosclerosis. A discussion of the clinical and nosologic relationship of parkinsonism to Foerster's arterio-

sclerotic rigidity, Jakob's type of senile rigidity with dementia, Alzheimer's disease and syphilitic mesencephalitis is not within the scope of this contribution. We shall limit our discussion to the type of parkinsonism that is symptomatic of cerebral arteriosclerosis.

As a rule, arteriosclerotic parkinsonism occurs in persons with evidences of peripheral and retinal arteriosclerosis, and the symptoms generally appear later in life than in the idiopathic type. Apoplectiform insults immediately preceding the development of the syndrome are not uncommon in cases with sudden onset. The clinical picture in some of these cases is identical with that described by Bechterew as "hemitonia" and by Boettiger as "hemihypertonia apoplectica," and is characterized by the occurrence of a preceding cerebral vascular accident, which is followed by the development of a parkinsonian syndrome on one side of the body. However, an insidious and slow onset of the disease is more common. Comparatively speaking, the progress of the disease is more rapid in arteriosclerotic than in idiopathic parkinsonism, and it may advance by a series of sudden exacerbations due to repeated apoplectiform insults.

Tremor and the "cog-wheel" phenomenon are not so common in the arteriosclerotic cases as in the idiopathic ones, and there is no excessive flexion of the hip and knee during walking; the steps are usually short; festination, propulsion, lateropulsion and retropulsion are rare. The muscles seem firmer to the touch. The rigidity is uneven in distribution and varies in extent. It is more marked in the muscles of the lower extremities than in those of the trunk and upper extremities. Critchley[2] stressed the fact that although the arteriosclerotic type of rigidity is characterized by difficulty in obtaining relaxation, it is nevertheless independent of the voluntary factor and still exists when all the volitional elements are removed. In advanced cases of arteriosclerotic parkinsonism the tendency toward catatonia is much greater than in idiopathic cases. In most of the arteriosclerotic cases there is little or no smoothing out of the wrinkles of the face, and phenomena referable to disturbances in the vegetative nervous system are far less common than in the idiopathic type, whereas bulbar symptoms (dysphagia, dysarthria, sialorrhea and bulbar speech) are more common in the arteriosclerotic type.

In the arteriosclerotic patients, psychic changes characterized by disturbances in memory and orientation, anxiety, irritability, periods of depression, emotional instability and explosive laughter and crying appear very early and are severe. Sphincteric disturbances, especially

2. Critchley, M.: Arteriosclerotic Parkinsonism, Brain **52**:23 (April) 1929.

incontinence, are also more common and appear earlier than in the idiopathic cases.

Valuable as the criteria thus far enumerated may be in the recognition of the arteriosclerotic type of parkinsonism, they are of only secondary diagnostic significance as compared with the association of a parkinsonian syndrome with symptoms and signs referable to focal cerebral or cerebellar disease. It is this association that may be said to be the pathognomonic feature of arteriosclerotic parkinsonism.

The greatest diagnostic difficulties, however, are encountered in cases of parkinsonism in which, although the patients are undoubtedly arteriosclerotic, the parkinsonian syndrome has made its appearance immediately after an infection of the upper respiratory tract or some other obscure febrile disease. In these cases the history and mode of onset of the disease, its clinical course, the presence of ocular signs, the greater degree of "greasiness" of the skin of the face and of other vegetative nerve phenomena, as well as the different types of mental disturbance, when such exists, in most instances will be of aid in determining the nature of the disease. In this connection, however, we must admit that we have had personal experiences in cases of this kind in which the final clinical diagnosis could not be established with any reasonable degree of certainty until the brain had been subjected to detailed histologic investigation, and even then there was some doubt as to the precise nature of the case.

A review of the literature of the cases of parkinsonism studied anatomically, as well as our own cases, will readily show that in a considerable number of cases the pathologist encounters considerable difficulty in making a pathologic diagnosis as to whether he is dealing with a case of encephalitic, idiopathic or arteriosclerotic parkinsonism. In many of these cases, unless the pathologist has some information as to the onset and clinical history of the case in addition to the anatomic observations, a positive pathologic diagnosis may be impossible. This is not surprising if one takes in consideration that in every one of the cases reported, as well as in our own, the pathologic process was one of diffuse involvement and hardly ever localized to sharply limited centers or groups of centers.

In our cases there were extensive chronic, diffuse, parenchymatous changes involving the pallidonigral system. The nucleus most constantly involved was the substantia nigra. In the three encephalitic cases this structure showed evidences of an extensive, chronic inflammatory process with marked gliosis; in the two idiopathic cases many of the pigment cells were destroyed, those remaining being swollen and depigmented; the destructive process in these two cases was not so marked as in the

encephalitic cases; there was no perivascular infiltration and no neuronophagia, and the glial proliferation was much less pronounced. In one arteriosclerotic case (case 7) the only change in the substantia nigra was the presence of arteriosclerotic vessels, whereas in the other arteriosclerotic case (case 6) the caudal portion of the substantia nigra showed no changes, but in its cephalic portion there was abundant glial proliferation with marked cellular destruction and much extracellular pigment; apparently the process here had already been arrested.

The fact of the anatomic connections of the substantia nigra with the precentral convolution, frontal lobe, pallidum, corpus luysii, pons and thalamus does not permit any conclusions as to which symptoms of the syndrome are to be attributed to involvement of the substantia nigra. In this connection it may be recalled that Jakob, as well as many other observers, described cases in which the akinetic-hypertonic syndrome was found with degeneration limited to the substantia nigra as the exclusive anatomic lesion. As a matter of fact, Jakob stated that tremor, pulsions and postural anomalies may be as marked in lesions of the substantia nigra as in lesions of the striopallidal system.

It is also noteworthy that in our cases the substantia nigra was as constantly involved in the idiopathic and arteriosclerotic cases as in the encephalitic ones, although, as was to be expected, the nature of the pathologic process was different in the different types.

The locus caeruleus was involved in every case, except in one idiopathic case. The extent of the involvement of this structure ran parallel to that of the substantia nigra. In two cases (cases 2 and 4), this structure seemed to be especially affected. We are not prepared to say whether these changes are of any significance. In case 2 the illness was characterized during life by especially severe symptoms referable to the motor fifth cranial nerve (grinding of the teeth).

The locus caeruleus is considered by some anatomists to be the site of origin of the mesencephalic root of the fifth nerve. The grinding of the teeth in case 2 perhaps may have been due to the severe involvement of the locus caeruleus. Such marked involvement of the locus caeruleus (substantia ferruginea) in the cases in which the substantia nigra was also severely involved also seems to suggest that this nucleus may perhaps have some relation to the pallidonigral system, especially if one bears in mind that the substantia nigra has long been regarded as the center for coordination of chewing and swallowing movements.

The pallidum was involved in every case, but most severely in the idiopathic and arteriosclerotic cases, and least in the encephalitic cases; in one of the latter (case 2) it showed only slight perivascular infiltration and some état criblé. The severity, extent and nature of the

lesions in the pallidum bore no relationship to the severity and distribution of the rigidity.

The putamen was most severely involved in case 4, an idiopathic case with marked tremor. The next severest involvement was in the two arteriosclerotic cases, in neither of which was tremor a conspicuous feature. Moderate involvement of the putamen was found in two encephalitic cases (cases 1 and 3), whereas in the third encephalitic case (case 2) the putamen was entirely normal. It was also moderately involved in the second idiopathic case (case 5). In all of our cases the severity and, to a great extent, the type of involvement in the putamen corresponded closely to that in the pallidum. There was no constant relation between the severity of the tremor and the severity of the lesion in the putamen except in one idiopathic case (case 4).

The thalamus was involved in every case, except in one encephalitic case (case 2) of twenty-two months' duration; in none of the cases, however, were the lesions very severe. Except for the presence of perivascular infiltration in the two encephalitic cases (in addition to the other changes described), there was little difference in the type of lesion in the various cases.

The hypothalamus was involved in only one case that was diagnosed clinically as encephalitic (case 1), perivascular infiltration and an increase in the subependymal glia being the principal observations. Although the vegetative nuclei surrounding the third ventricle, as well as the nuclei in Forel's field, showed severe cell changes in this case, the only clinical phenomenon referable to vegetative centers was an unusually "greasy face."

The corpus luysii showed various degrees of involvement. Lesions were found in every case except in one encephalitic case (case 3) and in one idiopathic case (case 4). Although the corpus luysii is connected anatomically with the substantia nigra and zona incerta and with the striatum and pallidum by way of the striosubthalamic fasciculus, the involvment of the corpus luysii bore a less constant relationship to that of the substantia nigra and a more constant one to that of the pallidum.

The red nucleus was involved in five cases. There were marked gliosis and moderate neuronophagia in one encephalitic case (case 1); slight perivascular infiltration in another encephalitic case (case 2); changes in the ganglion cells and slight état criblé in one idiopathic case (case 4), and moderate changes in the ganglion cells in the other idiopathic case (case 5). The most severe involvement in our entire series, characterized by a destruction of ganglion cells, neuronophagia, mild gliosis and vascular sclerosis, was found in one of the arteriosclerotic cases (case 6). The absence of cerebellar symptoms in all of these cases

in the presence of such marked involvement of the red nucleus—the outpost of the cerebellum—is noteworthy.

The fiber changes may be summarized as follows: In one encephalitic case (case 1) of six years' duration, there was a slight diminution of the fibers in the neostriatum, a marked diminution of the myelin sheaths in the anterior third of the lateral columns of the medulla with less severe degenerative changes in the remaining two thirds of the medulla and slight état criblé was also present in the pallidum, putamen, thalamus and substantia nigra. In another encephalitic case (case 3), the globus pallidus alone showed slight état criblé. In the third encephalitic case (case 2), of only twenty-two months' duration, no fiber changes and no état criblé were observed. In one idiopathic case (case 4) the lower third of the striopallidal fibers showed état criblé and état marbré, and slight état criblé was also found in the pallidum putamen and in and around the red nucleus. In the other idiopathic case (case 5), only very slight état criblé was seen in the pallidum. In one arteriosclerotic case (case 6) marked état criblé was found in the pallidum, putamen, thalamus, internal capsule and corona radiata. In the other arteriosclerotic case (case 7), état criblé was seen in the pallidum, neostriatum, thalamus and right internal capsule.

The severity of the fiber changes ran fairly parallel to the duration of the disease and to the degree of involvement of the ganglion cells, gliosis and vascular changes in the sections examined, the severest involvement apparently being in the two arteriosclerotic cases.

SUMMARY

To summarize the pathologic observations in our cases, we may say that the pallidonigral system was affected more constantly than any other part of the brain. The substantia nigra was involved in every case except in one diagnosed clinically as arteriosclerosis in which it showed only evidences of vascular sclerosis. The lesions in the locus caeruleus paralleled, to some extent, those in the substantia nigra. The pallidum seemed to have been mostly affected in the idiopathic cases. As to involvement of the other basal ganglia, it did not seem to make much difference whether the case was encephalitic, idiopathic or arteriosclerotic so far as the site of the pathologic process was concerned, the deciding factor being the nature of the process. It is noteworthy that in five of our cases in which the cerebellum was subjected to careful histologic examination, no lesions were found.

The changes in the cells were typical of a chronic degenerative process. From these alone, however, it was difficult to distinguish pathologically between the various types of parkinsonism, unless other factors,

such as the presence of perivascular infiltration or of arteriosclerotic changes, etc., were taken into consideration. It seems that the longer the duration of the disease, the closer does the histologic picture of the cells approximate that of the idiopathic type. In chronic cases the perivascular infiltration and the "Abbau" products in the Virchow-Robin spaces tend to disappear, the cells degenerate and are replaced by proliferated glia, and the myelin sheaths become destroyed, giving rise to état criblé and état marbré. In this connection we wish to point out that from our own work we do not know how much significance can be attached to état criblé (as described by the Vogts) as a pathologic observation in material that is examined so long after death as ours. As a fact, many competent modern neuropathologists deny the existence of état criblé. They attribute so-called état criblé to an artefact due to a dropping out of the blood vessels in the process of fixation in formaldehyde.

In two of our cases with clear histories of epidemic encephalitis preceding the development of the parkinsonism, the pathologic observations were extremely confusing; from the histologic picture alone it was impossible to determine whether the disease was inflammatory or degenerative.

Our cases seem to show also that the generally accepted view that the neostriatum and pallidum are the predominating sites for the lesions in idiopathic parkinsonism and the substantia nigra in encephalitic parkinsonism must not be adhered to too slavishly in attempting to differentiate pathologically between these two types of disease.

The diffuseness of the chronic inflammatory lesions in encephalitic parkinsonism, the extensive secondary changes in the brain following disease of the vessels in the arteriosclerotic and the widespread degenerative lesions in the idiopathic form make attempts to correlate the clinical picture with the anatomic observations an unusually difficult task. For similar reasons, cases of parkinsonism are of little value in the study of the pathophysiology of the various cardinal signs and symptoms of the syndrome.

Whereas the clinical course of the syndrome depends to a great extent on the nature of the pathologic process, it is obvious that its symptomatology does not depend entirely on the structural changes found in the nervous system after death. In this connection it may be well to recall that Renaud [3] reported three cases of chronic encephalitic parkinsonism with cachexia, each of about three and a half years' duration, in none of which was there any pathologic evidence

3. Renaud, M.: Sur trois autopsies de parkinsoniens post-encéphalitiques, Rev. neurol. **32**:57 (July) 1925.

of an inflammatory process. In these cases the blood vessels were normal; there were no "lacunae" of disintegration, no glial proliferation and no loss of medullated fibers. The only lesions that were found consisted of some slight changes in the cells to which the author attached no significance. Reports of similar cases are infrequently encountered in the literature. Jakob [4] also emphasized that in extrapyramidal disease the anatomicopathologic picture is by no means an absolute index of the clinical symptomatology. In this connection we may mention a case that was under the observation of one of us (M.K.) at the Mount Sinai Hospital.

A Russian Jew, aged 53, gave a history of weakness of the lower extremities, tremor of the left side of the body and twitchings of the left side of the face, coming on within five months before admission. On examination there was found a typical parkinsonian picture, with masklike facies, loss of normal associated movements, flexion attitude of the head, "cog-wheel" phenomenon in the left upper extremity, monotonous speech and fine tremors of the head and hands. In addition, there were bilateral pyramidal tract signs in the lower extremities and some ataxia in the left arm; the pupils were irregular, the left larger than the right, and both reacted poorly to light. The patient died of agranulocytosis eight months after admission. After a painstaking histologic examination the only pathologic changes found in the brain were in the inferior olivary nucleus.

It is also of interest that Guillain, Mathieu and Bertrand[5] recently expressed the opinion that all components of the parkinsonian syndrome —rigidity, tremor and hypokinesis—may be produced by a localized lesion of the inferior olivary nuclei.

Recently Wilson [6] also stressed that in some cases, age (senescence) has an effect on the general structure of a tissue, without giving rise to symptoms. "This," he said, "is true of Clark's column in the aged, and also for the cells in the striatum." More recently, the same author [7] also pointed out that there is no constant relationship between the size of a lesion and the extent of functional disturbance one may expect; hence, he said, "the symptomlessness of many a lesion found as a surprise at autopsy." Our cases, few as they are, seem to show that this is true not only of the extent of a lesion, but also of its nature.

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4. Jakob: Die extrapyramidalen Erkrankungen, Berlin, Julius Springer, 1923, p. 312.

5. Guillain, G.; Mathieu, P., and Bertrand, I.: Rigidity Originating in the Olives: Discussion of a Vascular Lesion of the Left Inferior Olive with Secondary Atrophy of the Right Olive, Ann. de méd. **25**:460 (May) 1929.

6. Wilson, S. A. K.: Modern Problems in Neurology, New York, The Macmillan Company, 1928, p. 184.

7. Wilson, S. A. K.: Deutsche Ztschr. f. Nervenh. **108**:4, 1929.

In the present state of knowledge there is altogether too little definite information as to the effects of disturbances of function and their relation to structural changes in the neural mechanisms as the basis of the symptomatology of the various diseases of the extrapyramidal system. This is especially true in parkinsonism. Hence the futility of attempting a definite differentiation between the various types of parkinsonism without taking into consideration the history, symptomatology, clinical course and pathologic observations. Practically, all one may say is that in many cases the presence or absence of certain signs or symptoms of parkinsonism during life will not always justify the clinician in giving an opinion as to what may be found at a postmortem examination. As a corollary to this, one may also say that without a knowledge of the symptoms and clinical course of the syndrome during the life of the patient the pathologist is not always in a position to reconstruct the clinical picture merely from an anatomic examination of the brain.

THE ORIGIN AND FORMATION OF SENILE PLAQUES *

ARMANDO FERRARO, M.D.
Research Associate in Neuropathology, New York State Psychiatric Institute and Hospital
NEW YORK

Senile plaques were first described in 1892 by Blocq and Marinesco,[1] who called them sclerotic plaques of neuroglia, a name which was later changed by Redlich [2] to miliary sclerosis. The term senile plaque was first applied to the lesion by Simchowicz.[3]

Since the first description of Blocq and Marinesco, numerous authors have tried to establish the significance as well as the pathogenesis of such a lesion. The fact that these plaques are found in the brains of normal senile persons has increased interest in their microscopic study. Furthermore, the fact that they are found in the presenium in that particular pathologic condition which was first described by Alzheimer in 1906, and since then has been known as Alzheimer's disease, has made the significance of these plaques more puzzling.

In regard to the histologic nature of the lesion, Blocq and Marinesco, in 1892, spoke of sclerotic plaques of neuroglia, a conception which was later emphasized by Redlich, and accepted also by Miyake,[4] Léri [5] (1906), Simchowicz (1911) and Bielschowsky [6] (1911). Alzheimer [7] also was in favor of the theory of the origin of senile plaques from the disintegrated neuroglia reticulum and from the deposit of an abnormal metabolic substance, a conception which was later accepted by Perusini [8] (1909-1911) and Ciarla [9] (1914) and partially admitted by Tumbelaka [10]

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2. Redlich, E.: Ueber miliäre Sklerose der Hirnrinde bei seniler Atrophie, Jahrb. f. Psychiat. u. Neurol. **17**:208, 1898.

3. Simchowicz, T.: Histologische Studien über die senile Demenz, Histol. u. histopath. Arb. ü. d. Grosshirnrinde **4**:267, 1910-1911.

4. Miyake, K.: Beiträge sur Kenntnis der Altersveränderungen der menschlichen Hirnrinde, Arb. a. d. neurol. Inst. a. d. Wien. Univ. **13**:212, 1906.

5. Léri, A.: Le cerveau sénile, Thèse de Lille, 1906.

6. Bielschowsky, M.: Zur Kenntnis der Alzheimerschen Krankheit, J. f. Psychol. u. Neurol. **18**:273, 1911.

7. Alzheimer, A.: Ueber eine eigenartige Erkrankung der Hirnrinde, Centrallbl. f. Nervenh. u. Psychiat. **18**:177, 1907.

8. Perusini, G.: Ueber klinisch und histologisch eigenartige psychische Erkrankungen des späteren Lebensalters, Histol. u. histopath. Arb. ü. d. Grosshirnrinde **3**:297, 1909-1910.

9. Ciarla, E.: Ein Beitrag zum histologischen Bild der senilen Hirnrinde, Arch. f. Psychiat. **55**:223, 1914.

10. Tumbelaka, R.: Zikte van Redlich-Alzheimer, Psychiat. en neurol. bl. **24**:1, 1920.

(1920), Bonfiglio[11] (1922), and Uyematsu[12] (1923). In 1925, Löwenberg[13] again emphasized the rôle of neuroglia in the formation of the plaques, adding that both protoplasmic and fibrous astrocytes and occasionally nerve cells and axis cylinders give origin to these structures.

In 1907, Fischer,[14] followed later by Fuller,[15] considered the plaque as the result of primary thickening of the axis cylinders.

In 1907, Gierlich and Herxheimer[16] looked on the plaques as derived from nerve cells, an opinion later accepted by Bonfiglio (1909), Ansalone[17] (1913), Vidoni[18] (1920) and Tumbelaka (1920).

In 1923, Uyematsu, although accepting the conception that the nuclear-like mass of the plaque is probably a product of disintegrated ganglion cells, said that he did not believe that all nuclear-like masses are remnants of degenerated nerve cells, because plaques were found in areas free from ganglion cells, as the outer layer of the cortex and the white substance.

The first attempt to consider the plaques as an expression of the involvement of the fundamental substance, that is, the intercellular substance which forms the background of the nerve tissue, was made in 1911 by Marinesco,[19] who expressed the belief that the origin of the lesion lies in a rupture of the colloidal equilibrium.

Sala,[20] in 1914, spoke also of a deposit of abnormal material, a point of view that was held by Ziveri,[21] (1912-1915) and by Frigerio[22] (1923).

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11. Bonfiglio, F.: L'anatomia patologica delle psicosi dell'età senile, Riv. sper. di freniat. **45**:219, 1922.

12. Uyematsu, S.: On the Pathology of the Senile Psychosis, J. Nerv. & Ment. Dis. **57**:1, 142 and 237, 1923.

13. Löwenberg, K.: Zur Histopathologie und Histogenese der senilen Plaques, Ztschr. f. d. ges. Neurol. u. Psychiat. **98**:549, 1925.

14. Fischer, O.: Zur Histopathologie der Presbyophrenie, Centralbl. f. Nervenh. u. Psychiat., 1908, vol. 19.

15. Fuller, L. C.: A Study of the Miliary Plaques Found in the Brain of the Aged, Am. J. Insan. **68**:147, 1911.

16. Gierlich N., and Herxheimer, G.: Studien über die Neurofibrillen in Zentralnervensystem, Wiesbaden, J. F. Bergmann, 1907.

17. Ansalone, G.: Contributo alla istologia patologica delle forme atipiche di demenza senile, Manicomio, 1913, vol. 28.

18. Vidoni, G.: Contributo allo studio delle placche senili, Quaderni di psichiat. **7**:113, 1920.

19. Marinesco, G.: Sur la structure des plaques dites séniles dans l'écorce cérébrale des sujets atteints d'affection mentales, Compt. rend. Soc. de biol. **70**:609, 1911.

20. Sala, G.: A proposito delle placche di Redlich-Fischer e dello sclerosi fibrosa dei vasi nella demenza presenile, Boll. d. Soc. med.-chir. di Pavia, 1914, vol. 27.

21. Ziveri, A.: Beiträge sur Kenntnis des präsenilen Irreseins, Ztschr. f. d. ges. Neurol. u. Psychiat. **8**:255, 1912.

22. Frigerio, A.: L'anatomia patologica delle psicosi senili, G. Federici, Pesaro, 1923.

In 1924, Tinel [23] expressed the belief that the elementary lesion from which the plaque originates is represented by a deposit of fatty acid, which is gradually transformed into an amorphous mass that is strongly argyrophile. Tinel's conclusions have been confuted by Rizzo,[24] who claimed that the fatty plaques are not pathologic formations, but the expression of artefacts due to prolonged fixation.

With the introduction of the new methods of silver impregnation attempts have been made to detect what rôle microglia and oligodendroglia play in the formation of the senile plaque. In 1922, Ley [25] expressed the opinion that in the formation of the plaque microglia elements take part as the result of reaction following the precipitation in situ of abnormal products of metabolism. Later, the astrocytes also react all around the plaque, but the reaction rarely leads to the formation of scar tissue.

Timmer [26] (1925) confirmed Ley's views and added that the Hortega cells have an important function in the development of the plaques. This conception was also admitted by Verhaart [27] in an article published in 1920.

In 1925, Urecchia and Elekes [28] expressed the opinion that the plaque originates from a primary necrotic involvement of oligodendroglial and microglial elements. Small plaques might originate from a single oligodendroglia cell. These authors believed that the axis cylinders also participate in the formation of the plaque, but that the reaction begins later.

Bolsi [29] (1927) confuted the views of Urecchia and Elekes, denying that the plaque originates primarily from nerve cells, glial elements or microglia. He thought that the primary alteration is represented by chemical modification of the interstitial fundamental substance which

23. Tinel, J: Les processus anatomo-pathologiques de la démence sénile, Rev. neurol. **2**:23, 1924.

24. Rizzo, C.: Le placche grassose nel cervello umano ed in quello degli animali, Riv. di pat. nerv. **29**:482, 1924.

25. Ley, R.: Étude anatomique sur la sénilité, Livre jubilaire de la Société belge de neurologie, 1922.

26. Timmer, A. P.: Der Anteil der Mikroglia und Makroglia am Aufbau der senilen Plaque, Ztschr. f. d. ges. Neurol. u. Psychiat. **98**:42, 1925.

27. Verhaart, W. J. C.: On the Development of the Senile Plaques in Alzheimer's Disease and other Senile Cerebral Diseases, etc., Acta psychiat. et neurol. **4**:399, 1929.

28. Urecchia, C. T., and Elekes, N.: Contribution a l'étude des plaques séniles. Bull. Acad. de méd. **94**:795, 1925.

29. Bolsi, D.: Sulla natura e genesi delle placche senili, Riv. di pat. nerv. **32**:257, 1927.

constitutes the medium surrounding the nerve elements. In the first stage of appearance the plaques are represented by primary small foci of argyrophile substance, and it is only later that chemical changes display a chemiotactic function calling into action the surrounding microglial elements.

Creutzfeldt and Metz [30] also believed in such an origin of the plaque, a view which was also accepted by Giacanelli [31] (1927).

Marinesco [32] (1928), in an interesting study of the origin and formation of senile plaques, reached the conclusion that they are due to precipitation of argyrophile substance resulting from a disturbed colloidal equilibrium. It is only following this precipitation that microglial elements are called into action, their presence resulting in an increase in the size of the plaque.

D'Ivry [33] (1927) added to the knowledge of the senile plaque the histochemical investigation of its central portion, reaching the conclusion that it discloses chemical properties common to amyloid substance, a fact accepted by Marinesco (1928) and Hechst [34] (1929). The conception of the latter is that the senile plaque originates from the deposit of amyloid substance at its center (which probably originated from disintegrated nerve cells), following which a microglial reaction occurs.

As may be seen from this rapid survey of the literature concerning the histogenesis of the senile plaque, no agreement seems to exist as to the origin of such a lesion; one group of investigators favors the theory that it originates from nerve cells, another, that it originates from the neuroglial elements, another, from axis cylinders, and still another, from the intercellular ground substance.

The purpose of my investigation has been, precisely, a study of the histogenesis of senile plaques independently from their distribution and correlation with clinical manifestations. In my studies I have used general staining methods: hematoxylin and eosin; the Nissl stain for nerve cells; the Bielschowsky stain for neurofibrils; the Hortega stain,

30. Creutzfeldt, H. G., and Metz, A.: Ueber Gestalt und Tätigkeit der Hortegazellen bei pathologischen Vorgängen, Ztschr. f. d. ges. Neurol. u. Psychiat. **106**:18, 1926.

31. Giacanelli, V.: Rilievi istopatologici e considerazioni sulla presbiofrenia, Ann. osp. psichiat. provin. Perugia, January-June, 1927.

32. Marinesco, G.: Recherches sur les plaques séniles, Bull. sect. scient. de l'Acad. roumaine **7-8**:1, 1928.

33. d'Ivry, P.: Étude histochimique des plaques séniles, J. de neurol. et de psychiat., 1927, vol. 9.

34. Hechst, B.: Zur Histochemie und Histogenese der senilen Plaques, Arch. f. Psychiat. **88**:126, 1929.

as modified by Globus and Penfield, for microglia and oligodendroglia; the Cajal stain for astrocytes; congo red for amyloid substance; the Best method for glycogen, and the fett ponceau for fat tissue.

HISTOLOGY OF THE SENILE PLAQUE

With the Nissl method, as well as with hematoxylin and eosin, no results of particular importance have been found differing from those usually seen with these methods, the plaques appearing as small roundish areas of disintegration in which no structure may be found. More interesting are the results that I have obtained by using the gold and silver impregnation methods for the study of neuroglia and microglia.

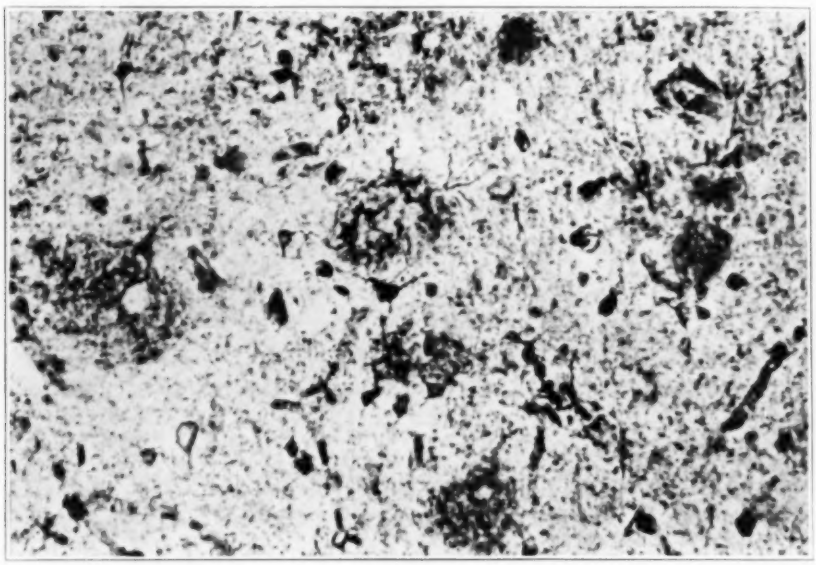

Fig. 1.—Senile plaques of various size, some of which are surrounded by cellular elements; Globus-Penfield modification of Hortega silver carbonate method.

The senile plaques vary in number and in size. Near large ones smaller ones are found, at times collected in a narrow area and at other times spreading into a larger surface. With the silver carbonate method it may already be seen under medium magnification that inside the plaques and surrounding them there are cellular elements, the nature and details of which I shall describe (fig. 1). At times these elements may be numerous and at other times scarce, only one or two cells being detectable in the middle of the plaque. At times these cells are compact, pressed together in the central portion of the lesion, and at other times they assume a radiating formation as in figure 2 *A*. At other times

only one side of the plaque contains cellular elements, while the remaining portion shows only residual cellular prolongations (fig. 2 *B*). With a higher magnification these cells are seen to represent both microglia and oligodendroglia, which can be detected either in the center or at the periphery of the plaque.

The microglia elements that are present have undergone pathologic changes, most of which are of a degenerative type. In figure 3, two microglia cells are seen occupying the central portion of a plaque. The cells are hypertrophic; the nucleus of one is somewhat vacuolated, and the prolongations of both are thicker and fragmented.

Figure 4 shows more pronounced degenerative changes of a microglia cell occupying the center of another plaque. At times the pathologic

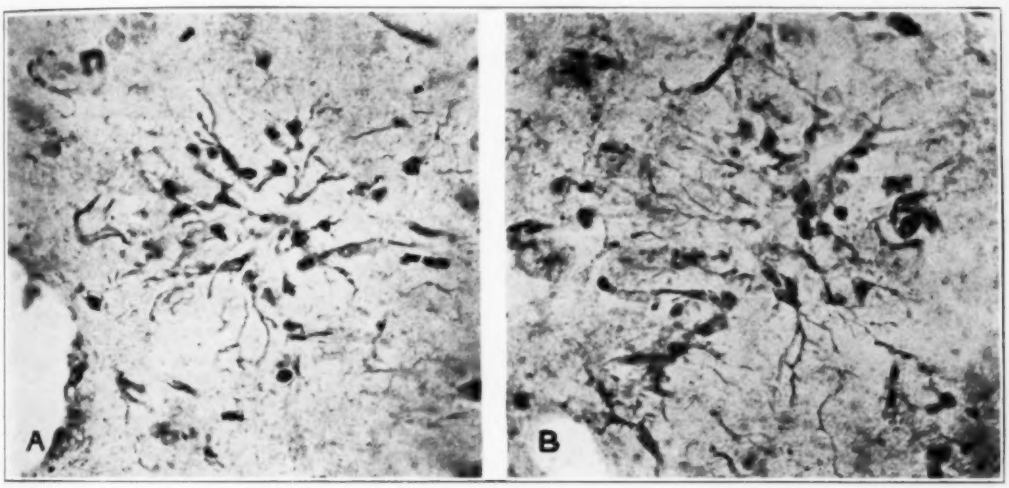

Fig. 2.—*A*, radiate disposition of cellular elements, constituting a senile plaque. *B*, cellular prolongations shown in a senile plaque. The right side of the plaque shows, however, various complete cellular elements. (Same method used as in figure 1.)

changes are pronounced, and the cell assumes huge proportions, as represented in figure 5. It may be seen here that while the central portion of the plaque is occupied by a huge microglial element, surrounding the plaque two swollen oligodendroglia cells are found. The central microglia shows thickened and enlarged prolongations, some of which are terminated by a masslike structure.

The microglia cells are not the only ones that may be found in the middle of a plaque; oligodendroglia cells may also be located in the central portion of some of the plaques and may be undergoing pathologic changes like the microglia. Figure 6 shows a distinct oligodendroglia cell, still well preserved and disclosing only slight hypertrophic changes.

Fig. 3.—Two microglia elements occupying the central portion of a senile plaque. The cells are undergoing degenerative changes. (Same method used as in figure 1.)

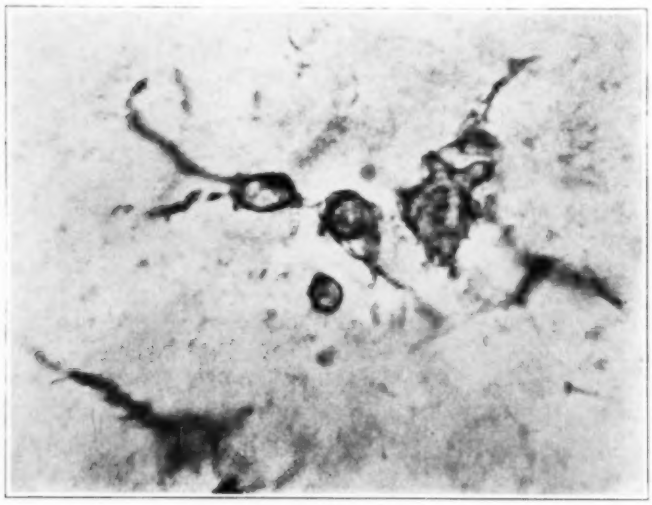

Fig. 4.—More pronounced degenerative changes of microglia elements. (Same method used as in figure 1.)

Figure 7 discloses in the central portion of another plaque an oligodendroglia cell in a condition of moderately acute swelling. Figure 8 discloses the presence of two oligodendroglia cells, one of which is undergoing degenerative changes in its prolongations.

It is certain, then, that both oligodendroglia and microglia cells are usual components of senile plaques. The pathologic changes that both elements undergo are of the nature of atrophic degeneration (von Meduna [35]), represented especially by shrunken elements with deeply stained nuclei. Some of the cells undergo a process of vacuolization that seems to be independent of the process of transformation into gitter cells. In this connection, I may mention that in rare instances gitter cells are found, either in the center or at the periphery of the plaque. With appro-

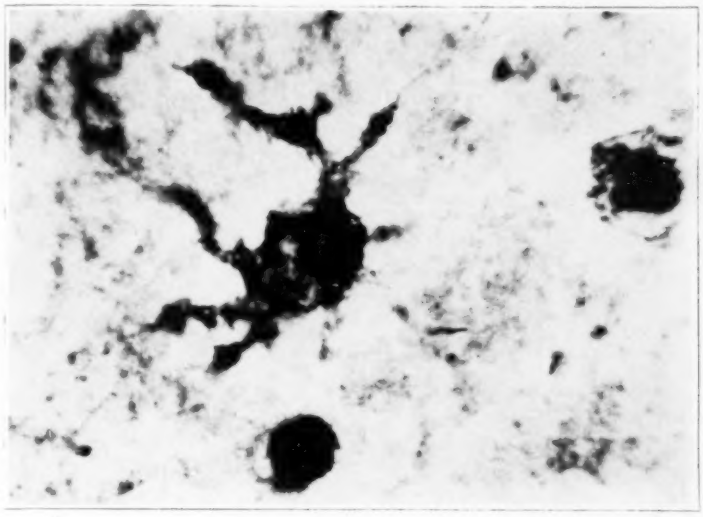

Fig. 5.—Considerably hypertrophied microglia all occupying the central portion of a plaque. (Same method used as in figure 1.)

priate counterstaining I have been able to detect a certain amount of microglial elements containing fat in both the cell body and the prolongations. Most of the elements disintegrate before they reach the round shape of gitter cells. My impression is that neither microglia nor oligodendroglia cells seems to possess enough vitality to carry on the valuable process of fat elaboration. The condition here is more of the nature of fatty degeneration of the individual elements than of an active process of "Abbau." Indeed, no gitter cells are found outside the plaque, thus pointing also to the absence of any migratory function of the fat-loaded elements.

35. von Meduna, L.: Beiträge zur Histopathologie des Microglia, Arch. f. Psychiat. **82**:123, 1928.

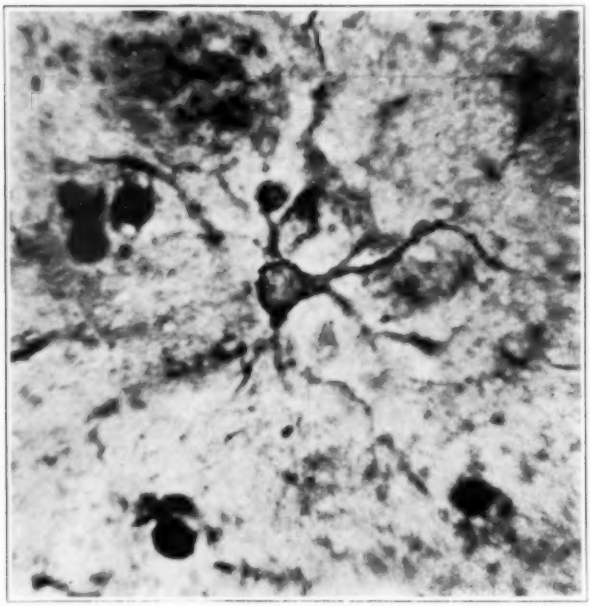

Fig. 6.—Oligodendroglia element, slightly hypertrophic, in the central area of a senile plaque. (Same method used as in figure 1.)

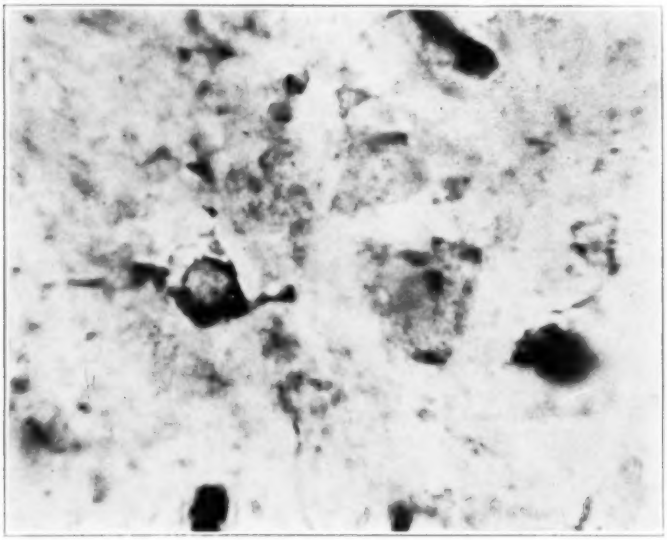

Fig. 7.—Oligodendroglia cell in a stage of partial swelling located in the center of a plaque. (Same method used as in figure 1.)

I must point out also that not all the plaques show fat-containing elements. In a large number of the plaques the microglia and oligodendroglia cells undergo gradually a particular process of granular disintegration, the nature of which it is difficult to establish. The process of disintegration leads to the formation of the granular amorphous substance which constitutes the argyrophile mass of the plaque. This consideration seems to me of importance as it establishes beyond doubt that both microglia and oligodendroglia participate in increasing the size of the plaque through their progressive disintegration. The cellular element that undergoes this particular disintegration can be followed for a long time until it gradually fades out in the fundamental granular substance of the plaque.

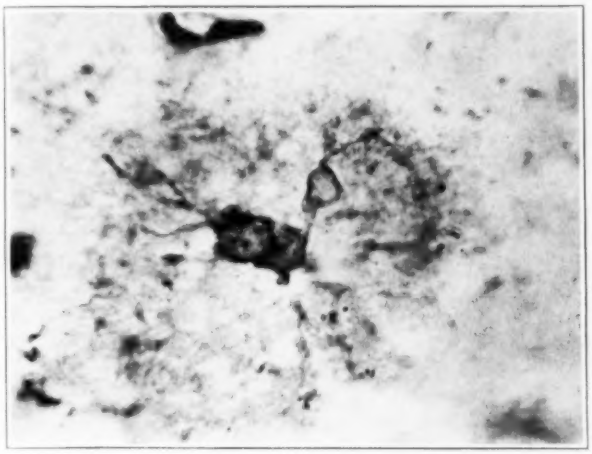

Fig. 8.—A cluster of two oligodendroglia cells undergoing degenerative changes. (Same method used as in figure 1.)

There are, then, two types of reaction of the microglia and the oligodendroglia; (1) fatty degeneration, the end-result of which is the disintegration of the element and the freeing of the fat substance which can be located free in the plaque; (2) the particular type of disintegration that leads to the granular destruction of the cell. It is the second type of reaction of microglia and oligodendroglia that contributes especially to the increase in the size of the plaque.

Histochemical methods show, as already pointed out, that the central portion of the plaque may be formed at times by fat tissue owing to disintegration of fat-degenerated cells. In other instances, by using the congo red and methyl violet methods, it has been possible to detect the presence of a substance that has some of the staining properties of amyloid. Not all the plaques contain this amyloid substance, as the internal layers of the cortex are generally free from it.

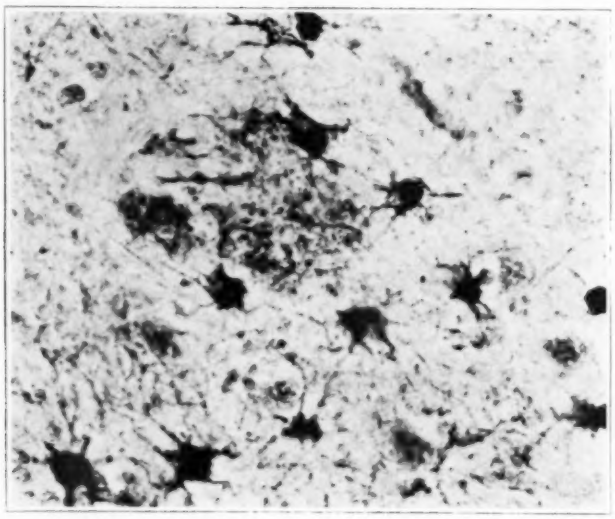

Fig. 9.—Astrocytes located at the periphery of a senile plaque: gold sublimate method of Cajal.

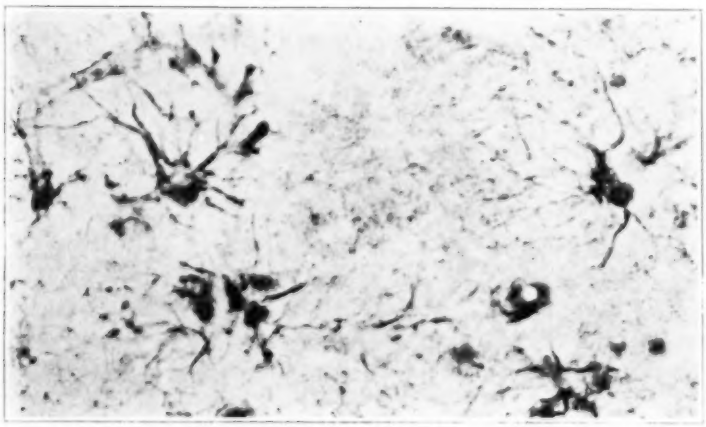

Fig. 10.—Astrocytes surrounding at a certain distance the contour of a plaque. (Same method used as in figure 9.)

The astrocytes are found in a condition of reaction (progressive or regressive) surrounding the plaques. The important fact about these is that, in general, they surround the plaque at a more or less considerable distance. At times, however, as in figure 9, the cells are closely located at the periphery of the plaque, while at others they are more distantly located, as in figure 10. Although this reaction of the astrocytes is most common, there are few plaques in which the astrocytes are found in the middle of the structure and undergoing a more or less advanced stage of degeneration. Figure 11 shows a plaque surrounded by a few astrocytes, two of which are located in the center and are undergoing degenerative changes. This establishes the possibility that astrocytes, although in a very small amount, contribute to the increase

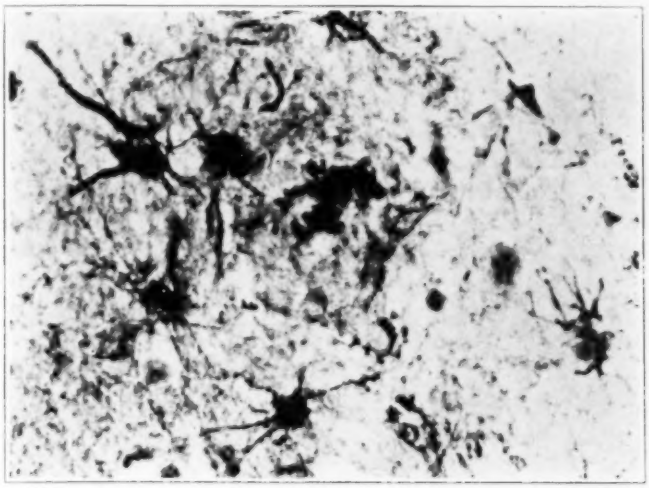

Fig. 11.—Astrocytes included in the middle of a plaque and undergoing degenerative changes. (Same method used as in figure 9.)

in size of the senile plaque through the disintegrated products resulting from their degeneration.

The astrocytes surrounding the plaque generally show changes of a progressive type, i. e., hypertrophy and hyperplasia, but it is also possible, as for instance in the external layers of the cortex, that some astrocytes undergo degenerative changes of the type of clasmatodendrosis (fig. 12).

Neurofibrils are seen in the plaque in a stage of more or less advanced disintegration. Figures 13 and 14 show swelling and fragmentation of the axis cylinder as detected by the Bielschowsky method. Some of the fragments are granular and others are considerably swollen. They all look thicker and deeply stained. At times it is not easy to differentiate between thick disintegrated axis cylinders and residual portions of prolongations of microglia or oligodendroglia.

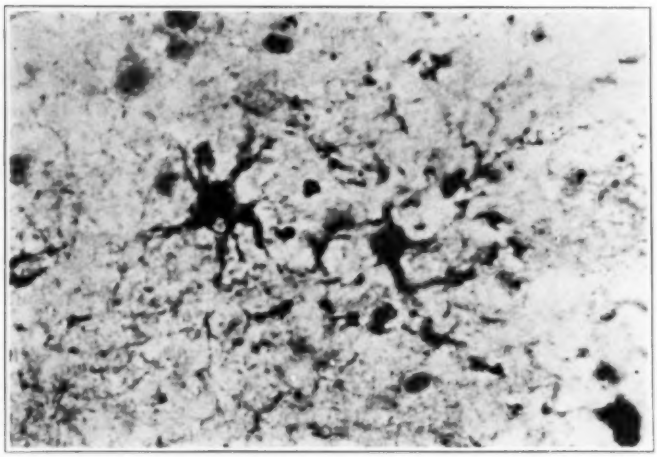

Fig. 12.—Pronounced clasmatodendrosis as astrocytes in the immediate vicinity of a plaque. (Same method used as in figure 9.)

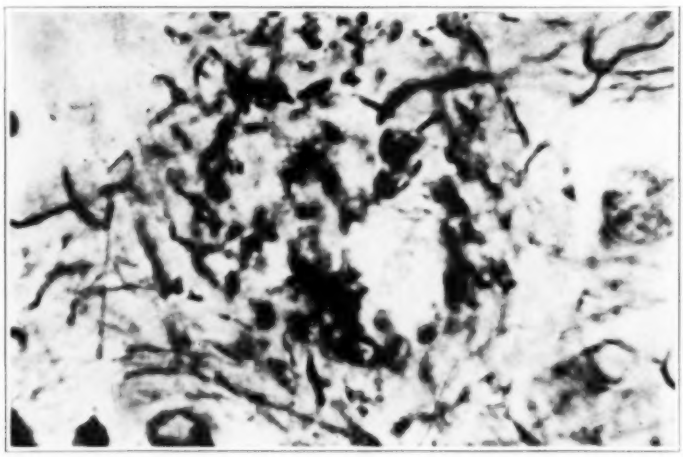

Fig. 13.—Fragmentation of axis cylinder in the center of a plaque; Bielschowsky method for neurofibrils.

I have been able to detect no regenerative changes (neurotization of the plaques) as recently emphasized by Marinesco.

HISTOGENESIS OF THE SENILE PLAQUE

In order to detect the primary origin of the senile plaque I have studied the minute plaques. This appears to be easier in three areas: the external layers of the cortex, Ammon's horn and the layer of Purkinje cells of the cerebellum.

I have detected at least two types of minute plaques that develop from an individual cellular element, the one from microglia or oligodendroglia and the other one from nerve cells. Figure 15 shows that in

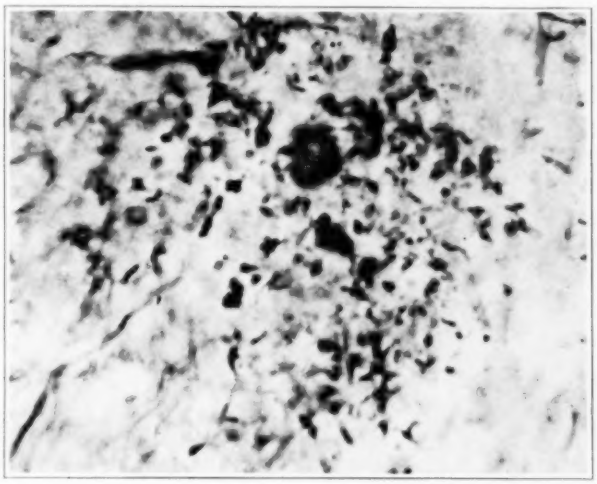

Fig. 14.—More pronounced fragmentation of neurofibrils in a senile plaque. (Same method used as in figure 13.)

the vicinity of a large plaque numerous others of smaller size are found; some are formed from one cellular element, represented in this particular instance by microglia and oligodendroglia. At times these minute plaques formed from individual elements are isolated and at others they are collected in more or less compact clusters in which the individuality of every plaque is, however, preserved. It is often possible with careful examination to detect the type of cell that is being transformed into a minute plaque. From a study of transitional stages, I have established that some of the larger plaques are formed by a fusion of individual minute ones. I am justified, then, in expressing the opinion that oligodendroglia and microglia cells may undergo a particular type of degenerative change, the nature of which is not as yet known, and constitute a small plaque or the origin of a larger one. Of these

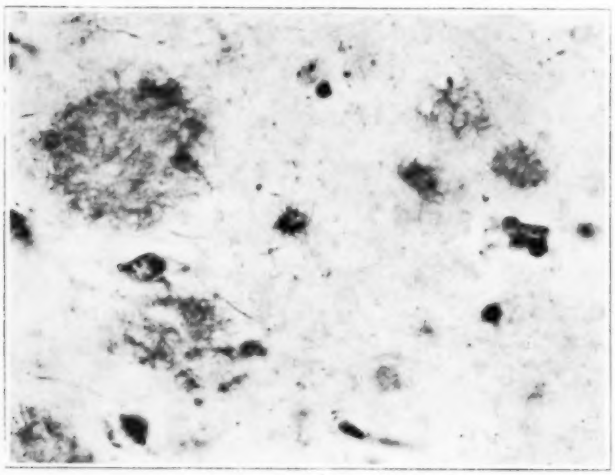

Fig. 15.—Minute monocellular plaques originating from single degenerated oligoglial or microglial elements; silver carbonate method. (Globus-Penfield modification.)

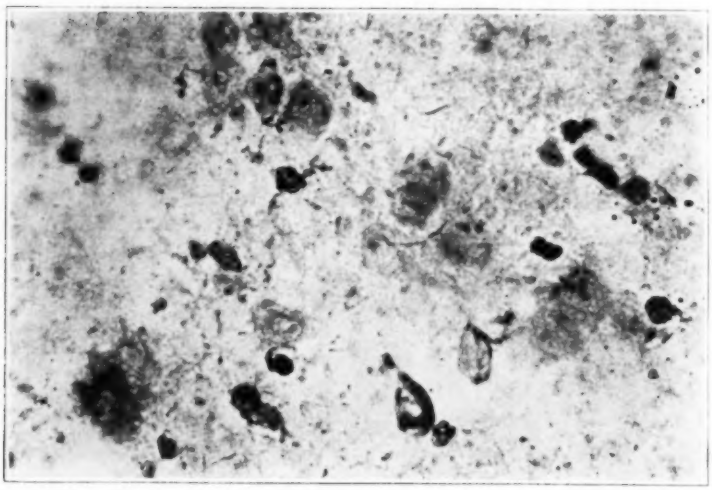

Fig. 16.—Minute monocellular plaques originating from single nerve cells undergoing disintegration. (Same method as in figure 15.)

cellular elements, the plaques originating from microglia are the more numerous.

Another source of origin of senile plaques is the nerve cells. I have no doubt that minute plaques develop from transformed individual nerve cells. Figure 16 shows this preliminary stage of disintegration. In this small plaque the cellular structure can still be recognized, especially the nuclear structure. I have often succeeded in identifying in the middle of an area disclosing more or less numerous senile plaques the occurrence of early plaques that developed from one or two cellular elements. At times, as is the case with plaques developing from microglia, a larger plaque is found formed by the accumulation of various

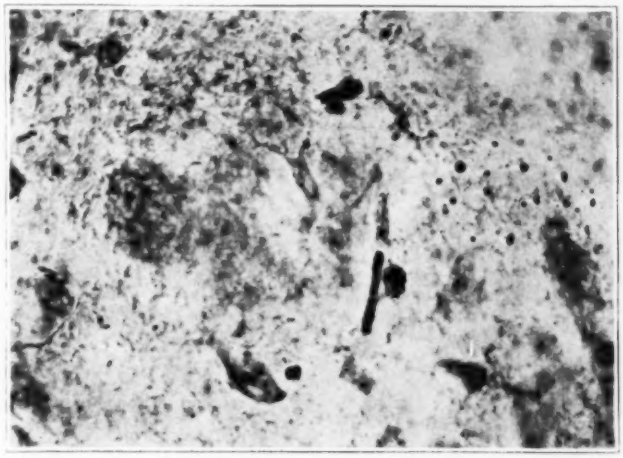

Fig. 17.—Nerve cell at the immediate periphery of a senile plaque, undergoing a process of disintegration similar to the one of the plaque itself. (Same method used as in figure 15.)

smaller units, each one still preserving morphologic characteristics that recall the original nerve cell. Figure 17 shows, at the periphery of an already formed senile plaque, a nerve cell that is undergoing a degenerative process of the same morphologic nature as the plaque. The cellular structure is still definitely noticeable.

In the cerebellum it can be seen beyond doubt that plaques originate from individual nerve cells. Figure 18 shows the occurrence of a few plaques in the lamina molecularis and in the layer of the Purkinje cells. Under a high magnification one can readily convince oneself that some of the plaques are derived from the transformation of an individual Purkinje cell. Figure 19 shows a typical plaque which, beyond doubt, is derived from a Purkinje cell; some of the dendrites of the cell are still detectable in the structure.

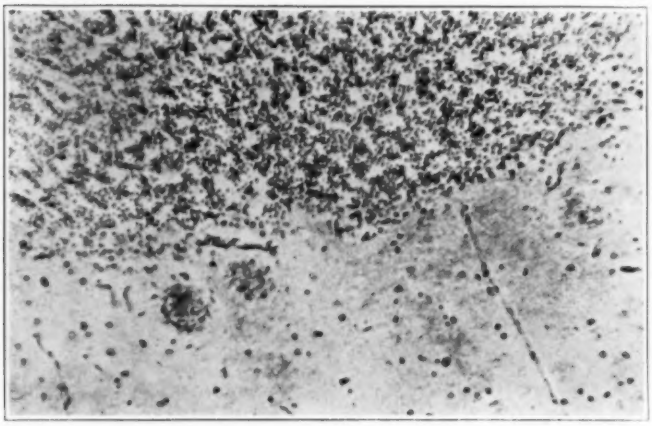

Fig. 18.—Senile plaque in the lamina molecularis and layer of Purkinje cells of the cerebellum. (Same method used as in figure 15.)

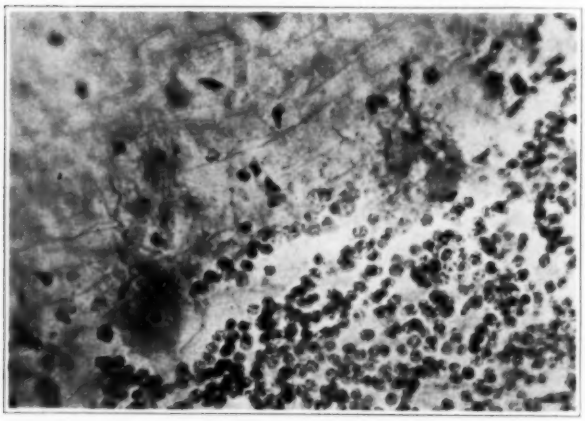

Fig. 19.—Purkinje cells undergoing a transformation into a monocellular plaque. (Same method used as in figure 15.)

From the various single elements forming very small plaques, larger plaques originate through the following mechanisms: Either numerous minute plaques fuse together to give origin to a larger plaque, or, surrounding the original minute plaque, a reaction of the oligodendroglia and microglia occurs leading to the degeneration of these elements, which will contribute to an increase in the volume of the original plaque. In this way, there are two possibilities of expansion: one that may be called the centrifugal type, in which development occurs from the center toward the periphery, and the other the centripetal type, in which development occurs from the periphery toward the center.

The fact that some plaques do not show cellular structures in the center has been advanced as an argument against the cellular origin of the plaques. I do not consider this objection a serious one, as some of the acellular plaques may originate from individual cells and thus have no other cellular structure, while the larger ones may be the result of an advanced stage of disintegration of the original element as well as of the cells of reaction (oligodendroglia and microglia) which have lost all traces of individuality.

I do not favor a division of the plaques into various types, as has been attempted by some authors. I believe that the mechanism of the formation of the plaque is fundamentally the same and that its morphologic structure is derived from the amount of reaction of the microglia and oligodendroglia as well as from the intensity of the process of degeneration. When the amount of microglial and oligodendroglial reaction to the original lesion is considerable, numerous hypertrophic prolongations of these various elements may be seen, giving to the plaque the impression of a radiating formation, the rays of which are formed by hypertrophic prolongations. The same might be said as to the type of plaque that has been called nuclear, meaning the division of the plaque into a central nuclear-like mass and into a peripheral ringlike formation. I believe that the nuclear appearance is due to the intensity of degenerative changes in the central portion leading to the formation of the characteristic amorphous and argyrophile central mass.

CONCLUSIONS

Senile plaques are formations that may originate from both neuroglial elements and from nerve cells. Of the neuroglial elements the oligodendroglia cells give origin to some of the plaques, while the astrocytes do not seem to participate in their histogenesis. Conversely, the microglia cells represent an important element from which senile plaques primarily develop. Senile plaques may also originate from isolated disintegrated nerve cells or from a collection of such elements.

The histochemical process that leads to the transformation of a cellular element into a senile plaque is as yet unknown. All that I can say is that it leads to the formation of a granular argyrophile substance which gives at times, in the central portion of the plaque, some of the reactions of the amyloid substance, and at other times the reaction of fat substance.

I have never seen nerve fibers giving origin to senile plaques.

Once the plaque is formed, its development in size and in volume depends on the participation of nerve cells, microglia, oligodendroglia and, less frequently, astrocytes.

Of the cells that do contribute largely to the development of the plaques, the microglia constitute the largest number.

The nerve fibers also participate in the development of the senile plaque through a process of fragmentation and gradual disintegration of the neurofibrils.

DISCUSSION

DR. J. H. GLOBUS: We have witnessed an excellent demonstration of the finer histology of senile plaques. Several years ago, I made a minor contribution on the subject of senile plaque formation. In a study of the reactive or degenerative changes of the central nervous system, particularly in cerebral arteriosclerosis, I have been able to show senile plaques, not in the conditions diagnosed during life as senile psychoses, but in persons who have had frank cerebral arteriosclerosis. I have found microglia contributing to the formation of senile plaques. It was my belief, at that time, that senile plaques were called into existence by changes in the blood supply in the region in which the plaques were forming. I have been able to show alongside, close to the periphery or in the center a small blood vessel, almost completely closed, and I thought that the slow closing of the blood vessel led to partial disintegration of the tissue, and that disintegration of tissue led to the mobilization of microglia, the prime purpose of which is to phagocytose dying tissue. Having reached that area, the microglia themselves fall victims to the poor vascularization of the invaded area, disintegrate and call on other microglia to carry away the products of disintegration. With this process the senile plaque grows as the cells, which are called on to carry away the products of disintegration, disintegrate themselves and lead to further accumulation of phagocytic elements.

DR. LEWIS D. STEVENSON: I am much interested in Dr. Ferraro's beautiful demonstrations of microglia and of senile plaques. I was interested to hear what Dr. Globus said, because it adds greatly to the discussion. In a case of Alzheimer's disease that I studied recently, I noted that the plaques stained much better with Hortega's silver carbonate than with Cajal's method, which stains the nerve cell elements, so that I concluded that the plaque was mainly made up of neuroglia elements. One thing that interested me was a Purkinje cell in the cerebellum which was breaking down and beginning to form a plaque. In a recent paper on the senile brain, the statement was made that Purkinje cells do not occur in senile plaques, but I have seen them there in one case and Dr. Ferraro has demonstrated that they occur. I believe that most of the microglia cells that were demonstrated were there as phagocytes.

DR. LOUIS CASAMAJOR: These remarkable slides illustrate Dr. Ferraro's points excellently, and they are beautiful examples of photomicrography as well as of technical preparations. My first experience with senile plaques was with Redlich; he stained them with the microglia stain, and obtained mere round purple spots in a yellow field, which he called *Druesen*, a term that is not particularly descrip-

tive. I have always believed, with Alzheimer, that they present miliary necroses, and the interesting point about them is the one which Dr. Ferraro stressed, and which Dr. Globus mentioned—the fact that this necrotic material is removed by the normal processes of removal, by gitter cells. Dr. Ferraro showed why that is. It is because the microglia also undergo a degenerative phase. These cells do not react like normal, living microglia in the presence of miliary necrosis, as would occur in the brain at an earlier age. I think that Dr. Ferraro's pictures of the microglia with the fat and amyloid stains are conclusive. They show that these cells are undergoing degeneration, and I cannot conceive of them as clearing-up cells. The fat they contain represents degeneration of their own protoplasm, and not an attempt at phagocytosis. The difference between the reaction of the oligodendroglia and the microglia, on the one hand, and the astrocytes, on the other, in the formation of senile plaques is rather an important point. It certainly gives some idea of the different nature of these two cells, as well as the difference in their origin. A striking point in the senile plaques is that in the presence of miliary necrosis there is no hyperplasia of the glia cells; the only cells that can make any attempt at phagocytosis are those already there, and they tend to undergo degeneration along with the other elements rather than hyperplasia, which is so necessary for defense.

The pictures of the cerebellum are very striking. Whatever one may think about the origin of the senile plaques in the cerebrum, no one can deny that senile plaques in the cerebellum come from degenerated nerve cells. Dr. Ferraro said that Alzheimer's fibroid degeneration occurred in some of these cells. One that he pointed out does not strike me as being particularly conclusive. I am interested in that point because in preparing slides for students I have had difficulty in securing those which showed both Alzheimer's degeneration and senile plaques. Some material shows well the Alzheimer degeneration, but as a general rule in those sections the senile plaques are few and far between. While it is much easier to find senile plaques than Alzheimer degeneration, I find many slides with senile plaques scattered through them in large numbers, and yet these sections are singularly poor for the Alzheimer degeneration. I have always thought that there must be two more or less distinct processes, and certainly the Purkinje cells have not undergone the Alzheimer fibrillar lesion. Again, as I remember, Simchowicz found senile plaques in a number of brains of old animals; while he found senile plaques in old horses, I do not recall that he found the Alzheimer alteration in any of the lower forms, so that although I feel convinced that the origin of the senile plaque is in the degeneration of the nerve cell, I still do not feel convinced that that degeneration of the nerve cell is of the nature of the fibril alteration of Alzheimer. These things seem to be two different and distinct processes, although belonging to the main process of a change in the brain as a whole.

DR. BORIS KWARTIN (by invitation): Does Dr. Ferraro think that one could consider the argentophilic granules the result of a combination of fatty acids with various mineral bases, forming soaps? Apparently, as a result of the necrosis, fatty acids are freed from their chemical combinations in the cells and might readily combine with various basic ions. Changes of this sort are observed in atherosclerosis.

DR. AMANDO FERRARO: Concerning the conception of Dr. Globus that the senile plaque may be the result of nutritional disturbances occurring in the immediate vicinity of the blood vessels, I am not against it. This is a possibility which has, as a matter of fact, already been taken into consideration by Uyematsu, who spoke of a perivascular type of senile plaque, and by Lowenberg, who described plaques occurring in the blood vessels of the white substance. The point to be considered mainly is whether the nutritional changes influence primarily the nerve cells, the neuroglia cells or the fundamental interstitial substance. My investigations lead to the conclusion that the lesion is primary in the nerve cells, the microglia or oligodendroglial elements. I think that few astrocytes are primarily

involved; these show more reactive phenomena of the progressive and regressive types.

Concerning the localization of the plaques, I can confirm Dr. Stevenson's report of senile plaques in the cerebellum. Besides, I have found them also in the basal ganglia, which agrees with the recent report of Baumann.

In regard to the phagocytic function of the microglia, I subscribe to Dr. Casamajor's opinion that microglial elements are not performing here the function of "Abbau" in the senile plaque and that one is dealing here with dominantly degenerative changes. I also agree with Dr. Casamajor as to the conception that Alzheimer's fibrillary disease and senile plaques are two distinct and independent pathologic processes. Nevertheless, in one case I have been able to find nerve cells with Alzheimer's disease undergoing degenerative changes leading to the formation of a minor plaque. I have found, as in Dr. Stevenson's case, areas in which both Alzheimer's fibrillary disease and the senile plaques were distinctly impregnated by the silver method.

In regard to the chemical composition of the plaque, I am in no position to discuss this at present, although the view expressed that fatty acids and mineral bases will form soap precipitating the silver may be correct.

ENCEPHALOPATHIA PERIAXIALIS DIFFUSA (SCHILDER'S DISEASE)*

CHARLES DAVISON, M.D.
AND
WILLIAM SCHICK, M.D.
NEW YORK

Cases of encephalitis periaxialis diffusa (Schilder's disease) have been frequently reported. Were it not that in the present case there were unique features of clinical and pathologic importance, its presentation would be omitted. The disease in this patient was diagnosed clinically, and at autopsy pathologic changes were found that were rarely observed in the other cases reported. A more complete review of the literature is given by Schilder,[1] Stewart, Greenfield and Blandy,[2] Krabbe,[3] Bauman,[4] Brock, Carroll and Stevenson [5] and others.

REPORT OF CASE

History.—B. T., an American girl, aged 15, of Italian parentage, was admitted to the Montefiore Hospital with the complaints of poor vision, mental deterioration, convulsive seizures and weakness of the extremities on the left side. She had been of average intelligence and well until she reached the fourth grade, when she became backward mentally. The first sign of illness was a convulsive seizure one and a half years before admission to the hospital. It was confined to the left side of the body and was accompanied by conjugate deviation of the head and eyes to the left, and clonic spasm of the limbs; it lasted for thirty minutes and was followed by stupor. She did not froth at the mouth nor bite the tongue, and she was not incontinent. She was well for the next six weeks, when she had another similar seizure. Following this she forgot things easily, became backward at school and found difficulty in performing simple calculations. The family was advised to discontinue the schooling. A third seizure followed shortly after the second. At this time she asked silly questions, performed apparently purposeless acts, exploded in spells of absurd laughter and complained of headaches.

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* Submitted for publication, May 26, 1930.
* Read at a meeting of the Neuropathology Club, Dec. 26, 1929.
* From the Neuropathological Laboratory and Neurological Division, Montefiore Hospital.

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3. Krabbe, K.: A New Familial Infantile Form of Diffuse Brain Sclerosis, Brain **39**:74, 1916.
4. Bauman, L.: Encephalitis Periaxialis Diffusa, Brain **47**:452, 1924.
5. Brock, S.; Carroll, P. M., and Stevenson, L.: Encephalitis Periaxialis Diffusa of Schilder, Arch. Neurol. & Psychiat. **15**:297 (March) 1926.

In June, 1928, she showed poor mentality and had a left hemiparesis with corresponding pyramidal tract signs. Vision was good. The veins of both fundi were congested, and questionable atrophy was present in the right papilla. The left side of the body showed diminution of all forms of sensibility. Gradually, the condition became worse. The weakness of the extremities on the left side grew more severe. She had spells of inane laughter and occasionally cried. Some of the seizures were associated with loss of consciousness; some were preceded by visual auras of colors, and on one occasion she complained of seeing "the devil." Later she found walking difficult. Although incontinence was absent, she had to urinate frequently. Appetite was great. The surroundings were no longer recognized, and she was slightly disoriented. For a few weeks before admission she now and then complained of smelling "ether." At times she gave expression to a fear that her aunt would kill her.

With the exception of the fact that a brother was backward in school, the family history was unimportant. Nothing was known of the birth and early development of the patient. During childhood she had measles.

Physical Examination.—The child was well developed and nourished; she sat quietly in bed until approached, when she laughed unnecessarily and spasmodically. Speech was poor and nasal. She gave evidence of marked motor unrest, bit the examiner's fingers, pinched his hands and flung herself and her right arm about violently. Her expression resembled that seen in Wilson's disease. A nasal spur protruded from the left portion of the septum. She had marked arching of the hard palate. All other organs appeared normal in the general examination. Her blood pressure was 105 systolic and 68 diastolic.

Neurologic Examination.—The gait showed a broad base with abduction and stiffness of the left lower extremity. Both feet were in the equinovarus position, the left more so than the right. The left upper extremity was flexed at the elbow and wrist and adducted at the shoulder joint. The metacarpophalangeal joints were flexed and the interphalangeal joints extended. The gait was uncertain and hesitant, and both lower extremities tended to be circumducted in hemiplegic fashion, the left more so than the right. Athetoid movements in the left hand appeared when the patient was forced to walk without help. There was some ataxia on the left side and also clumsiness in diadokokinesis. The outstretched left hand showed movements resembling pseudo-athetosis in the fingers. She recognized things and indicated their uses, although at times a good deal of difficulty was evinced in recalling their names. When the proper word was mentioned by the examiner she laughed approvingly.

The deep reflexes were hyperactive bilaterally, much more so on the left. Inexhaustible patellar and ankle clonus was present on the left, as well as the Babinski and confirmatory signs. An occasional suggestive extensor response was present on right plantar stimulation. The lower abdominal reflexes were exhausted easily. Voluntary power on the left was diminished. When the arms were outstretched, the upper part of the left arm lagged and the lower part was everted. The spasticity was marked in both extremities on the left side, more so in the lower. It was reducible voluntarily and did not show the cogwheel phenomenon. Sensation showed some diminution to all forms on the left side, but the cooperation of the patient was too poor for a proper evaluation of this observation. Smell could not be tested. Visual acuity was poor, but fingers could be recognized at 3 feet (0.9 meters). Colors were also recognized. The fields were restricted, and there was a suggestive left homonymous hemianopia. The fundi showed intense bilateral primary optic atrophy. The pupils were equal, regular

and dilated, and they reacted poorly to light and in accommodation. A supranuclear palsy of the seventh nerve was present. On voluntary innervation the palate rose poorly, but when she laughed it rose slightly better. Intellectual impairment was marked. She showed memory defects for recent and remote events, disorientation and a lack of insight into her condition. At times she voiced a fear that she would be "killed" by members of the house staff.

Laboratory Data.—All laboratory tests gave negative results, except for the observation of a faint trace of albumin in the urine.

Course.—During the stay in this hospital she had one typical jacksonian seizure, not associated with loss of consciousness. There were oculocephalogyric spasms to the left, with clonic movements of the left upper and lower extremities, twitching of the face and nystagmus to the left lasting for four minutes.

On Aug. 5, 1929, 150 cc. of spinal fluid was withdrawn by the lumbar route and replaced with an equivalent quantity of air. The resulting encephalogram

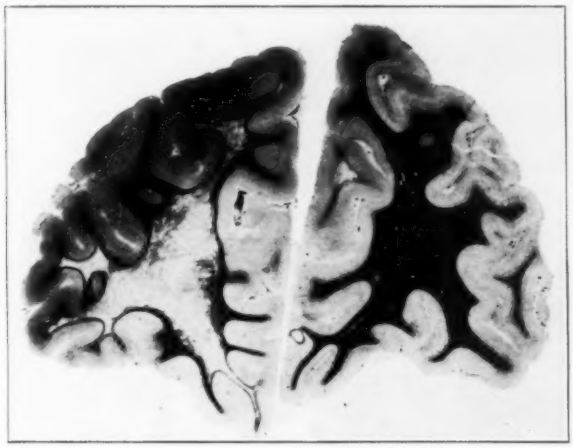

Fig. 1.—Vertical section of the frontal lobe showing demyelinization of the white fibers of the centrum ovale on the right. The arcuate fibers are spared; Weil stain.

showed general internal hydrocephalus. Following this, the signs and symptoms of meningitis developed. A spinal tap revealed the presence of 50 cells with a sterile fluid. Following the injection of air the patient was much depressed. She spent part of the day flinging the right upper extremity over the left shoulder and back. She was resistant to examination and objected to any manipulation, especially of the head. The temperature, which was elevated and showed irregular fluctuations following the ventricular insufflation of air fell to normal within a few days.

A centrifugated specimen of the spinal fluid, removed during the encephalographic procedure, showed clumps of large cells with pink cytoplasm and large irregular nuclei. Some of these were filled with blood pigment. They resembled ependymal cells.

On the morning of August 27, the pulse was rapid. Generalized tonic spasms developed, during which both lower limbs were severely extended, the feet being in marked equinovarus positions, the upper extremities adducted at the shoulders,

the arms flexed, and the forearms and wrists flexed and pronated. The pupils were dilated and rigid. The reflexes were difficult to obtain because of the marked increase in tonus throughout. A high temperature and violent tachycardia, which were followed by pulmonary edema, ended in death.

Postmortem Examination.—Macroscopic: The right hemisphere was somewhat smaller than the left. The pia-arachnoid had a glistening appearance and the convolutions were normal. At the base of the brain the pia-arachnoid was cloudy, thickened and slightly adherent to the sixth nerve. The brain was cut vertically in slabs 1 cm. in thickness. The entire ventricular system was uniformly enlarged, slightly more so on the right. The most outstanding feature was the marked enlargement of the third ventricle (fig. 2*A* and *B*). All coronal sections of the right side of the brain presented a grayish, translucent and tough appearance of the white matter. In the region of the right diencephalon all the structures appeared shrunken, especially the putamen and globus pallidus (fig. 2*A*).

Fig. 2.—*A*, vertical section through the diencephalon showing demyelinization of practically all the white fibers on the right with sparing of the arcuate fibers; involvement of the putamen and globus pallidum; thinning and demyelinization of the corpus callosum; patchy demyelinization on the left side; generalized hydrocephalus with marked enlargement of the third ventricle. *B*, vertical section in the region of the mesencephalon showing complete demyelinization of the white fibers on the right, partial demyelinization on the left, and erosion of the ependyma of the right lateral ventricle; Weil stain.

The section in the region of the hippocampus and mesencephalon presented the same picture, with a partial destruction of the brain substance and ependyma of the right lateral ventricle (fig. 2*B*). These sections showed a slight translucency and induration of the centrum ovale of the left central, postcentral, parietal and temporal convolutions. The sections of the parieto-occipital lobes showed the same picture with the exception that marked induration and translucency involved the white matter of both hemispheres. The sections of the occipital lobe at the tip of the posterior horn of the lateral ventricle presented a translucency and toughness of the white matter on the right side, with a faint involvement of the

Fig. 3.—*A*, vertical section of the cerebrum through the atrium ventriculi showing bilateral demyelinization of the white fibers with sparing of the arcuate fibers. *B*, vertical section through the tip of the occipital horn of the lateral ventricle showing partial demyelinization of the white fibers, with greater involvement on the right side; Weil stain.

white matter on the left. Sections at the tip of the occipital lobe showed induration and grayness of the white matter, mostly on the right side. The cerebellum, pons, medulla oblongata and spinal cord did not show any gross abnormalities.

Microscopic: Complete vertical sections of the cerebrum, pons, medulla oblongata and spinal cord from the regions described were embedded in celloidin, cut and stained by the Weil, hematoxylin and eosin, van Gieson, Mallory phosphotungstic and cresyl violet methods. Small sections from the white and gray matter of the frontal, precentral, postcentral, parietal, temporal, hippocampal and occipital convolutions, globus pallidus and putamen, pons, medulla oblongata, spinal cord and optic nerves were stained by the sudan IV, Weil, Cajal gold

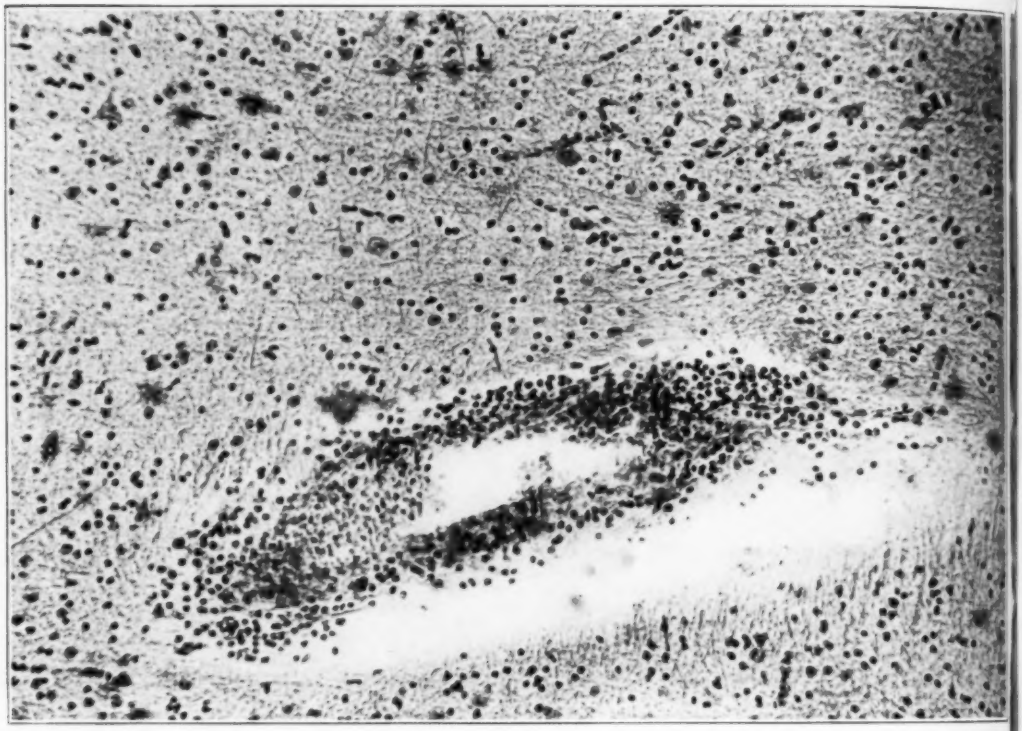

Fig. 4.—Perivascular edema and cellular infiltration. Bielschowsky stain; reduced from × 120.

sublimate, Rio-Hortega for microglia and oligodendroglia, Bielschowsky, Victoria blue, Mallory phosphotungstic and hematoxylin and eosin methods.

Sections through the frontal lobes (fig. 1) showed an almost complete demyelinization of the centrum ovale of the right side. Under higher magnification this indurated area, with the exception of a few broken-down and beaded myelin sheaths near the cortex, was completely devoid of myelin. The arcuate fibers, as observed in all slides, appeared fairly well preserved, but under higher magnification showed partial destruction of the myelin. The striking picture in the demyelinated areas in this and other sections was the perivascular edema and the marked infiltration of the adventitial spaces by compound granular corpuscles and

a few glia nuclei (fig. 4). With hematoxylin and eosin some of the compound granular corpuscles took a deep stain and had the appearance of lymphocytes. Others were larger, oval and vesicular, with little chromatin material, and resembled the endothelial type of cell. The perivascular spaces of the vessels in the involved regions were infiltrated with the same type of cells (figs. 4 and 5). With special stains, evidences of plasma cells in these spaces could not be demonstrated. The walls of the blood vessels did not show any marked changes except for the perivascular infiltration.

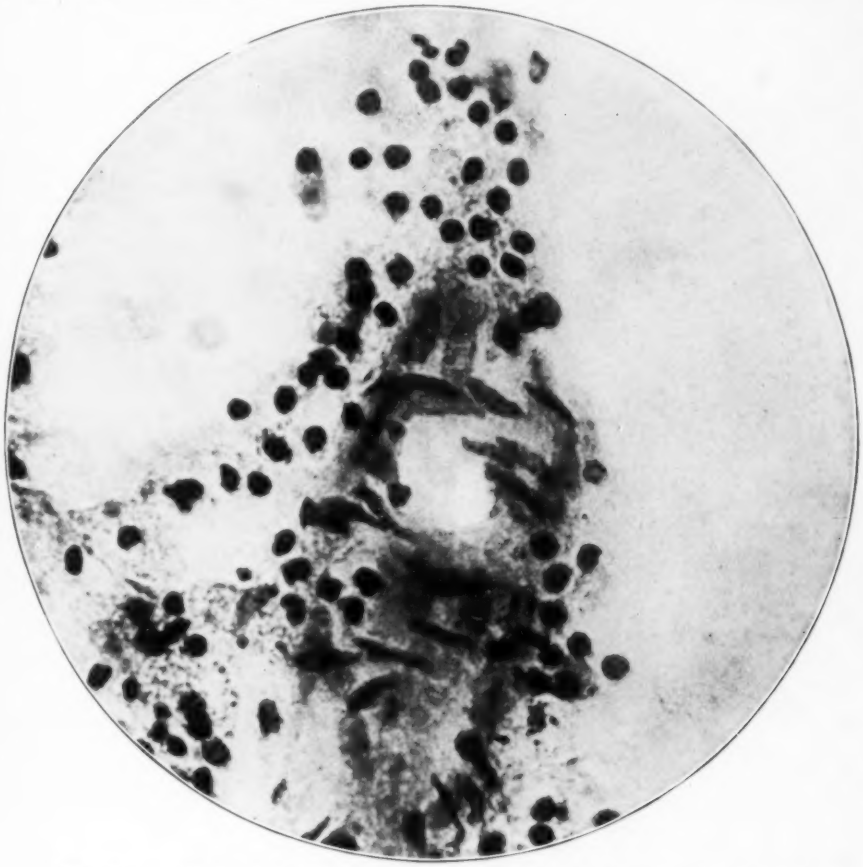

Fig. 5.—Proliferated endothelial cells and glia nuclei; hematoxylin and eosin; × 400.

The pia-arachnoid in this section, as well as that in other sections, showed thickening in places, consisting primarily of proliferation of fibroblasts with occasional apparent lymphocytes and compound granular corpuscles. With hematoxylin and eosin and cresyl violet the cortical layers did not show any alterations. The architectural arrangement of the cell layers was fairly well preserved, and with few exceptions all the nerve cells were normal. In places, part of the cortex near the arcuate fibers showed occasional vessels filled with compound granular corpuscles. With cresyl violet mitotic division of the glia was occasionally observed.

With sudan IV staining of the same material the perivascular spaces showed an accumulation of compound granular corpuscles and some nuclei which resembled lymphocytes. With higher magnification the apparent round cells showed slight traces of fatty granules in the periphery of the deeply stained nuclei (fig. 6). Proliferation of the endothelium was also noticed. There was a striking resemblance between the endothelial cells of the zones outside the perivascular spaces and the proliferated endothelial cells of the vessels. These endothelial

Fig. 6.—Accumulation of compound granular corpuscles in the perivascular spaces; sudan IV stain; × 300.

cells did not show traces of the fatty granules seen in the cells already mentioned. Conglomerations of compound granular corpuscles were observed not only in the perivascular spaces, but also in the rest of the demyelinated area. With the Bielschowsky method the perivascular edema and infiltration in the demyelinated area were very prominent (fig. 4). In some areas the axis cylinders stained poorly (fig. 7); in others they were partially destroyed. The few that were preserved were in a fragmented state and thickened, with ball-like terminations, and had

a corkscrew-like appearance. In the arcuate fibers the axis cylinders were fairly well preserved. With the same stain the cell bodies of oligodendroglia and microglia were observed. With the Victoria blue and Mallory phosphotungstic stains the destroyed areas were replaced by a fairly dense network of neuroglia in which many glia nuclei, varying in type and size, were enmeshed. With the Perdrau method, young fibroblasts growing out of the perivascular spaces and invading the adjacent demyelinated areas were well brought out. With the Cajal

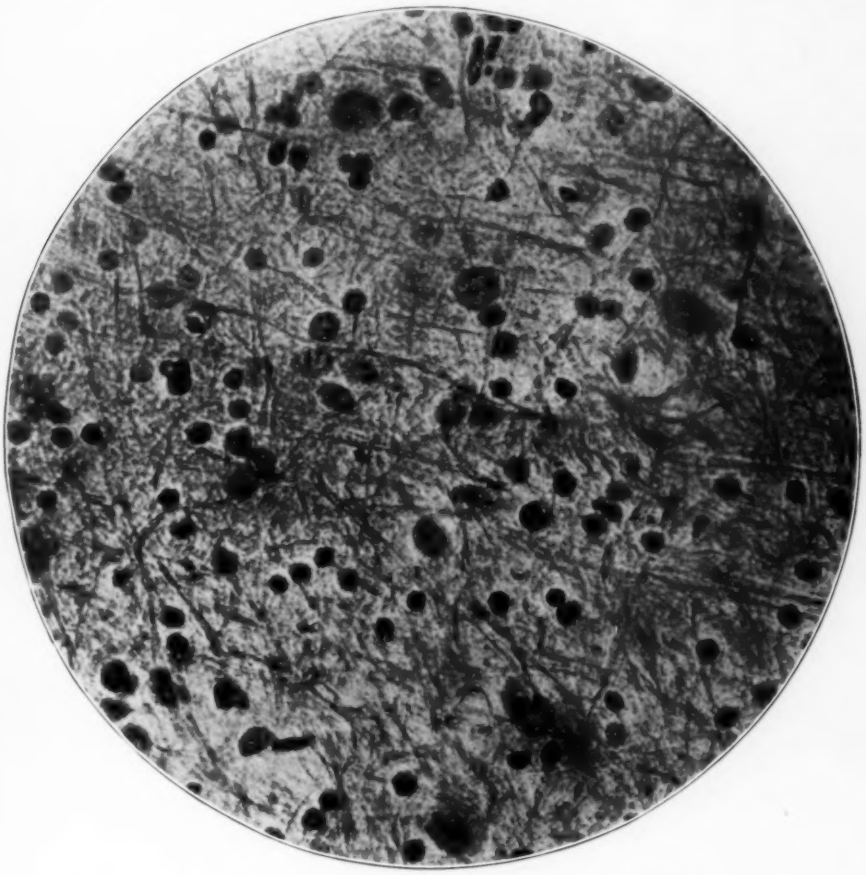

Fig. 7.—Axis cylinders taking the silver stain poorly; Bielschowsky stain; × 360.

gold sublimate stain the demyelinated area consisted of giant astrocytes mixed with numerous compound granular corpuscles and enlarged microglia that were being transformed into compound granular corpuscles (fig. 8). In the areas in which the demyelinization was less marked the astrocytes had larger processes which reached to the walls of the blood vessels (fig. 9). With this stain the cells in the perivascular spaces appeared as clumps and resembled the compound granular corpuscles seen in the sections stained with sudan IV. Microglia and

oligodendroglia nuclei, some of which were surrounded by a fair amount of cytoplasm, were found in abundance.

In the Weil preparations of sections that passed through the diencephalon (fig. 2*A*) an almost complete demyelinization of all the white fibers with partial sparing of the arcuate fibers on the right side was observed. The white matter of the fiber system of the right putamen, globus pallidus and corpus callosum was also involved. The corpus callosum not only showed demyelinization but was markedly thinned out bilaterally. The pons in the same section showed a slight demyelinization which was descending in type. On the left side the demyelinization was patchy and involved fibers coming from the postcentral, temporal and hippocampal gyri. With a higher power, the changes were the same as those

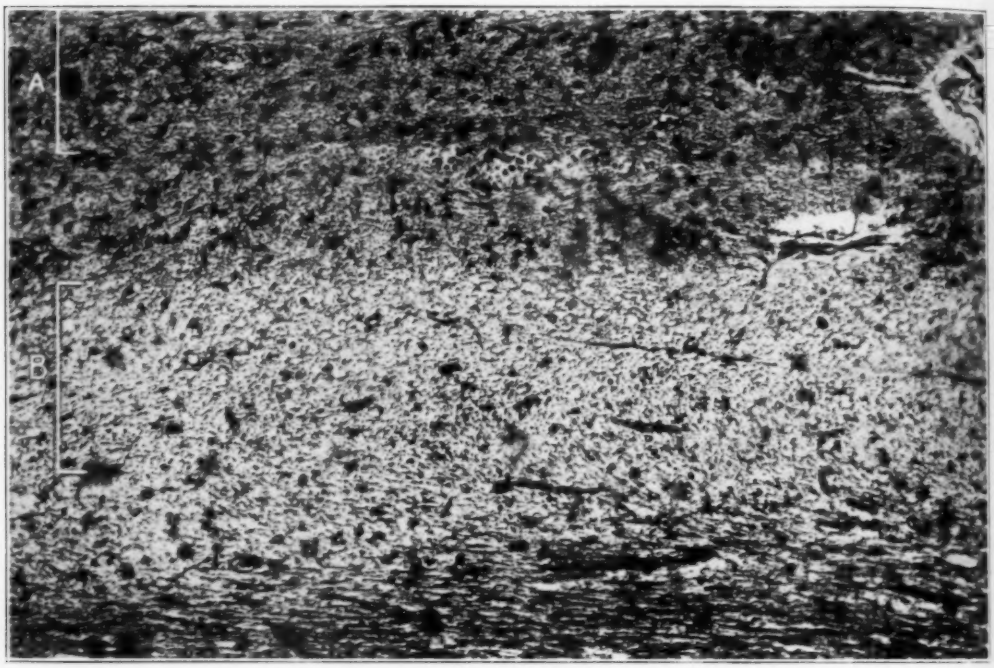

Fig. 8.—Astrocytic wall (*A*) near the destroyed area (*B*) consisting of protoplasmatic astrocytes, microglia and compound granular corpuscles; Cajal gold sublimate stain; × 120.

found in former sections. The sections of the right putamen and globus pallidus revealed the same changes, with the exception that some of the nerve cells, especially the smaller cells of the former, showed various destructive changes, such as chromatolysis, atrophy, neuronophagia and satellitosis. The damage to the nerve cells found in the right basal ganglia was less than that to the white substance of the same areas. The glial elements in the sections, with the exception of the ependyma, showed numerous microglia and oligodendroglia.

Sections of the cerebrum in the region of the mesencephalon (fig. 2*B*) showed a process similar to that observed in the previous sections, with the exception that the greater part of the ependyma of the right lateral ventricle showed erosion

and destruction. With a higher power, the ependymal lining was totally absent and the subependymal tissue showed the same changes as those observed in the white matter, except that the microglia and oligodendroglia were numerous (fig. 10), indicating a recent pathologic process. With sudan IV, the accumulation of fat within the perivascular spaces and the subependymal tissue proper was marked.

The pontile fibers on the right side showed a descending demyelinization and a slight increase in the glia nuclei.

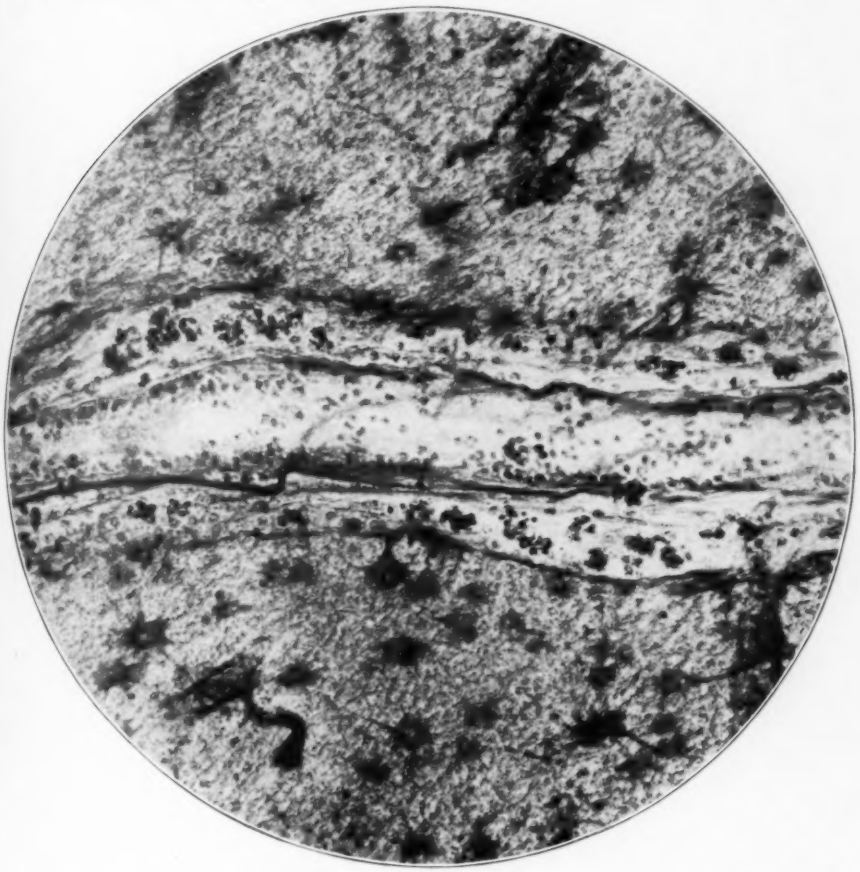

Fig. 9.—Numerous astrocytes in the demyelinated area; their processes reach to the walls of the blood vessels. Note the clumps of compound granular corpuscles in the perivascular spaces; Cajal gold sublimate method; × 400.

In sections of the brain through the atrium ventriculi (fig. 3*A*), a bilateral and fairly uniform demyelinization of the fibers of the centrum ovale coming from the postcentral and temporal convolutions was observed. The arcuate fibers were fairly well preserved, and the detailed microscopic pictures conformed to those of the previous sections except that the perivascular spaces and the white

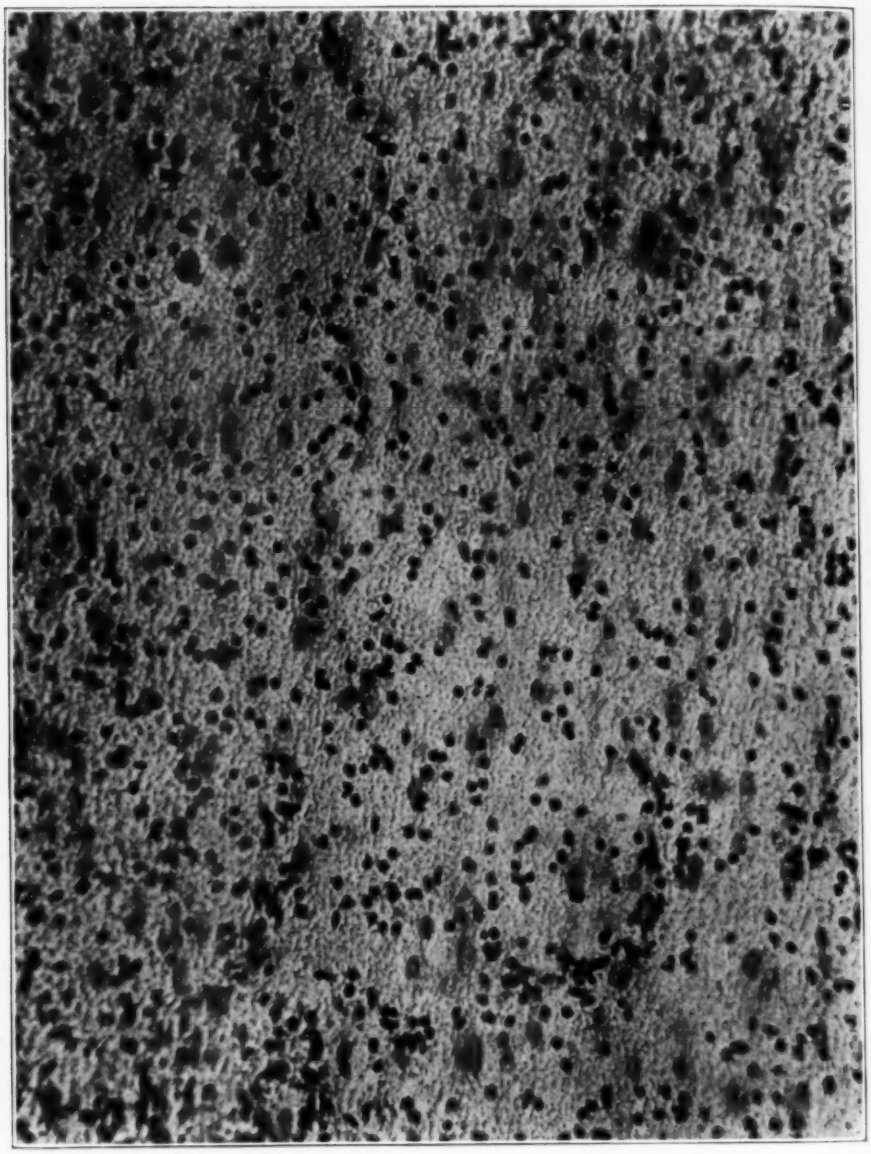

Fig. 10.—Section showing a field of oligodendroglia and microglia in the destroyed ependyma; cresyl violet stain; × 150.

matter on the left side did not show as marked an accumulation of compound granular corpuscles. The fibrillary astrocytes were more numerous in these sections.

Sections through the end of the occipital horn of the lateral ventricle showed a greater demyelinization on the right side, with patchy involvement on the left (fig. 3*B*). On the right side the fibers from the calcarine fissure showed moderate involvement (fig. 11), while those from the left calcarine fissure were fairly well preserved. The rest of the histopathologic changes were the same as those in previous sections.

Frozen and celloidin sections of the optic nerve and chiasma were stained by the same methods. With the Weil method, some of the fibers showed complete demyelinization (fig. 12); in others the myelin sheaths were swollen and fre-

Fig. 11.—Demyelinization in the calcarine area; sparing of the stripe of Gennari and arcuate fibers; Weil stain; × 60.

quently disintegrated. With hematoxylin and eosin some of the vessels showed accumulations of round cells about them which proved to be compound granular corpuscles and varieties of endothelial cells. The sheath of the optic nerve was thickened and infiltrated with the same type of cells as those found in the vicinity of the blood vessels. The Bielschowsky method showed partial destruction of the axis cylinders and fragmentation (fig. 13).

Sections through the cerebellum and medulla oblongata with the Weil method did not show demyelinization of the white fibers. However, with a higher magnification, occasional vessels showed an accumulation of compound granular corpuscles within the perivascular spaces and a slight increase in the glial elements of the white fibers. The latter were especially marked in the restiform body and in the vicinity of the right tenth and twelfth nerve nuclei. The nerve cells revealed minor changes. Occasionally a nerve cell showing vacuolization, swelling

and shrinkage, as well as chromatolysis, was found. Considering the marked changes that took place in the white matter, the changes in the nerve cells were almost negligible.

Sections of the lower portion of the medulla oblongata showed descending bilateral demyelinization of both pyramids, the right more than the left. The pia-arachnoid of the cerebellum and medulla oblongata showed considerable thickening, with an increase in the fibroblasts and an accumulation of round cells.

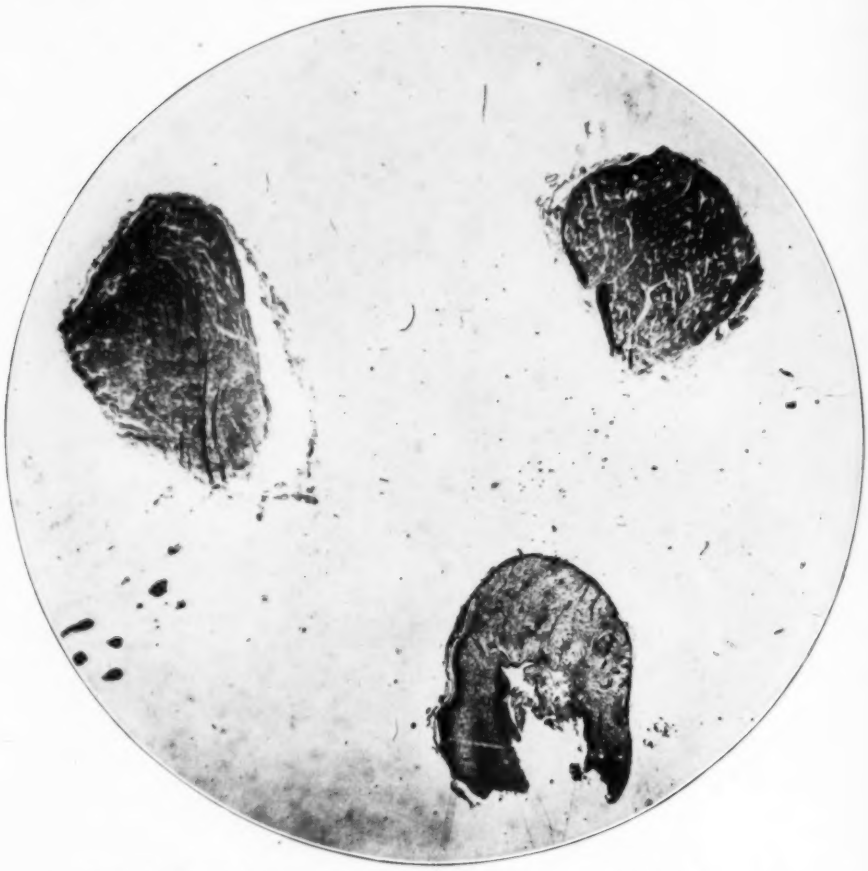

Fig. 12.—Partial demyelinization of the optic nerves; Weil stain; × 30.

Sections of the spinal cord at various levels, stained by the same methods, showed nothing of note with the exception of a descending demyelinization of the crossed pyramidal tracts and a slight proliferation of the pia-arachnoid, with an occasional accumulation of fibroblasts and round cells.

COMMENT

The case presented a typical picture and course, as described by Schilder, Greenfield and others. The unusual clinical features were

the marked signs of extrapyramidal disorder and the bilateral optic atrophy. Pathologically, the striking features were: the bilaterality of the process, which was more marked on the right and extended from the

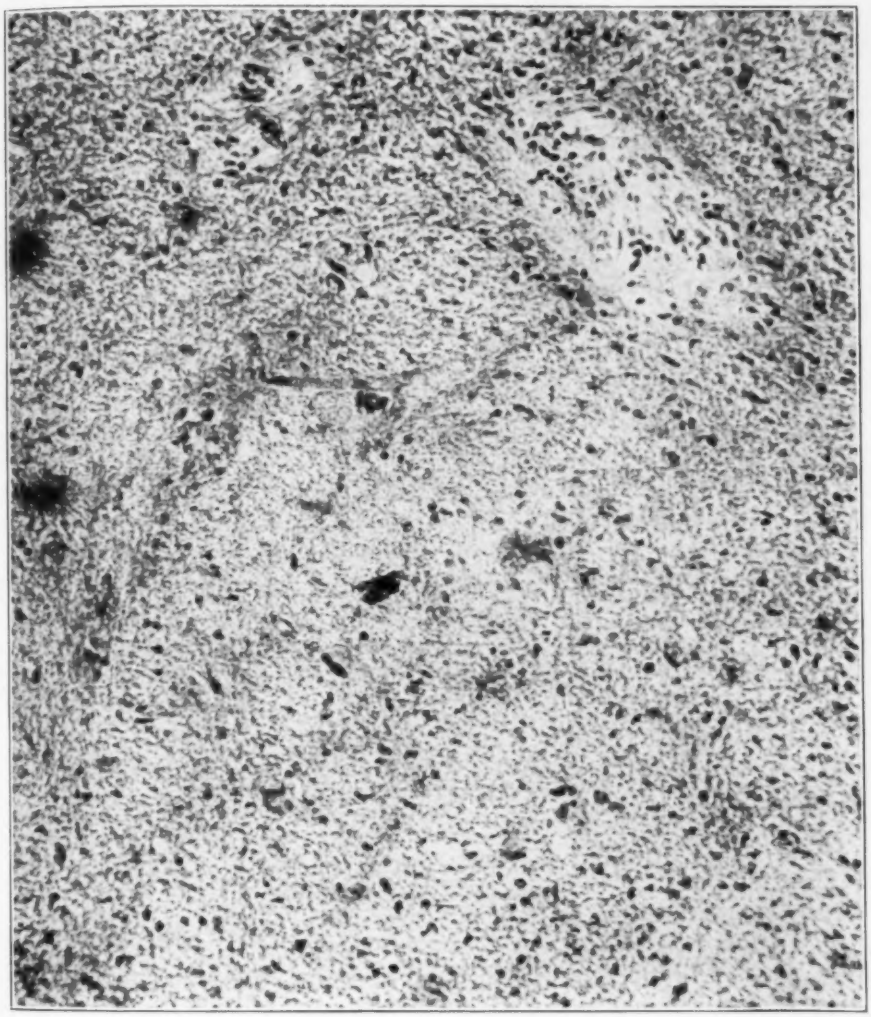

Fig. 13.—Destruction of the axis cylinders in the optic nerves (transverse section); Bielschowsky stain; reduced from × 150.

frontal to the occipital poles; the involvement of the corpus callosum and the optic nerves; the marked destruction of the ependyma on the right, as well as some of the nuclear masses, such as the right putamen, globus pallidus, thalamic and subthalamic nuclei.

The extrapyramidal disorders were corroborated by the finding of lesions in the nuclear masses and fiber tracts of the putamen and globus pallidus. Implication of these structures was found in: the case of Claude and Lhermitte,[6] in which both lenticular nuclei and the optic thalamus were involved; case 1 of Globus and Strauss;[7] a case of Jacob,[8] with a lesion of the left caudate nucleus; Hernel's case;[9] case 2 of Schroeder,[10] etc. In our case some of the thalamic and subthalmic nuclei were not free from lesions, and the damage to these structures may be the explanation for the spasmodic laughing, although this may also be accounted for by the marked damage to both cerebral hemispheres that is associated with the type of laughing observed in idiots, which the disorder in our patient more closely approximated.

Changes in the fundi have been described in a few cases, although pathologic studies have not been reported by many. Clinical reports of fundal changes are found in the cases described by Krabbe,[3] case 2 of Globus and Strauss,[7] the case of Rochon-Duvignaud,[11] and case 1 of Stewart, Greenfield and Blandy.[2] Stewart, Greenfield and Blandy[2] (case 2), Stauffenberg[12] and Shelden, Doyle and Kernohan[13] described the pathologic changes in the optic nerves.

We are not aware that any description of ependymal erosions has been given, with the exception of Globus and Strauss'[7] mention of a subependymal reaction. At one time the free ependymal cells found in the cerebrospinal fluid were considered to be tumor cells. The breaking down of the ependyma (fig. 2 *B*) in the anterior horn of the lateral ventricle was probably due to the marked destruction and reaction of the adjacent tissue, as evidenced by the presence of numerous microglia and oligodendroglia cells, an indication of a recent process.

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6. Claude and Lhermitte: Leuco-encéphalite subaigüe à foyers succesifs, Encéphale **15**:89, 1920.

7. Globus and Strauss: Progressive Degenerative Subcortical Encephalopathy, Arch. Neurol. & Psychiat. **20**:1190 (Dec.) 1928.

8. Jacob: Zur Pathologie der diffusen infiltrativen Encephalo-Myelitis in ihren Beziehungen zur diffusen und multiplen Sklerose, Ztschr. f. d. ges. Neurol. u. Psychiat. **27**:290, 1915.

9. Hernel: Ueber einen Fall von Encephalomyelomalacia clinica diffusa bei einem vierjahrigen Kinde, Deutsche Ztschr. f. Nervenh. **40**:436, 1910.

10. Schroeder: Encephalitis und Myelitis, Monatschr. f. Psychiat. u. Neurol. **3**:146, 1912.

11. Rochon-Duvignaud; Jumentié, and Valière-Vialeix, L.: Foyers multiples d'encéphalite intéressant les radiations optiques (Société de Neurologie), Rev. neurol. **30**:73, 1923.

12. Stauffenberg: Ein Fall von Encephalitis periaxialis diffusa, Ztschr. f. d. ges. Neurol. u. Psychiat. **39**:56, 1913.

13. Shelden, W. D.; Doyle, J. B., and Kernohan, J. W.: Encephalitis Periaxialis Diffusa, Arch. Neurol. & Psychiat. **21**:1270 (June) 1929.

Concerning the type of reaction observed in this disease, the patient described, the observation in another case from this laboratory reported by Kraus and Weil,[14] as well as a review of the cases in the literature, induce us to lean strongly to the idea that this is a toxic process. The major histopathologic observations conform to those in degenerative diseases of the nervous system. The occasional mild inflammatory reactions about the vessels or meninges, as evidenced by the presence of round, plasma and endothelial cells, which other authors describe, do not invalidate the views presented. Evidences of inflammatory reactions are occasionally encountered in degenerative diseases and tumors of the central nervous system, but these do not form the major picture. We therefore agree with Globus and Strauss that the process is primarily toxic, and that the histopathologic observations conform to those seen in degenerative and toxic processes of the central nervous system. What the noxious substance is, how it spreads, and why it picks primarily the white substance of the central nervous system cannot be stated definitely. Bauman was of the opinion that the white matter is supplied by the long vessels coming from the base of the brain and that the noxious substances travel only by this route. Such a view is untenable. A toxin that travels only through the long vessels and spares those which supply the arcuate fibers and cortex can hardly be conceived. That the cortex and arcuate fibers are not completely spared is shown in our case and in cases reported by others, although it is definitely established that the brunt of the injury is suffered by the fibers of the centrum ovale or the long fibers of the white matter.

As to the name for the disease, Globus and Strauss are correct when they attempt to label it in accordance with its pathologic picture. The only error in calling it "subcortical encephalopathy" is that in the true sense the process does not involve the subcortex alone. As shown in this instance and in cases presented by others, the cortex and other gray masses may also be involved. For this reason we chose the term of "encephalopathia periaxialis diffusa." There is a great deal to be said against the use of this term; but it was thought that since the disease entity described by Schilder is already known as encephalitis periaxialis diffusa, the use of the new term, which tends to describe the pathologic observations, will not introduce confusion into the discussion of a disease that has already been labeled and recognized as such. The disease was named encephalopathia periaxialis because the process is not inflammatory. It should also be emphasized that the bulk of the axis cylinders are involved, and the few that do not show marked changes take the special stains poorly.

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14. Kraus, W. M., and Weil, A.: Encéphalite périaxiale diffuse (type Schilder), Encéphale **9**:775, 1928.

SUMMARY

A case diagnosed during life as Schilder's disease is presented. The unusual features in this case were: intense optic atrophy, of a degree that led many to doubt the diagnosis; extrapyramidal disorders, with definite pathologic changes similar to those found in the rest of the white matter and an ependymal erosion and subependymal reaction. The term encephalopathia periaxialis diffusa is descriptive of the actual pathologic process observed.

DREAMS AND THEIR RELATIONSHIP TO RECENT IMPRESSIONS *

WILLIAM MALAMUD, M.D.
AND
FORREST E. LINDER, A.B.
IOWA CITY

The scientific value of data obtained in psychiatric research depends primarily on the validity of the methods used and the degree of accuracy with which their reliability can be determined. Here, as in all other branches of medicine in which methods are devised primarily for practical purposes, it is of special importance to have some means of determining whether a given method that has been shown to be practically useful can also be relied on in scientific research. There is no doubt, of course, that procedures originally introduced as empiric aids in diagnosis and treatment for disease may subsequently prove to be of definite use in scientific investigation. But this is not invariably so, and for this reason the validity of a method in this respect should not be taken for granted. The importance of such discrimination can be appreciated only when one considers the difference in the interests and the immediate purposes of those who represent these two aspects of medicine. For the person who is interested mainly in obtaining practical results, any method that offers useful leads to the diagnosis of the pathologic process in an individual case or helps in the treatment can also be applied in dealing with other similar cases. For the experimental investigator, however, whose interests lie in the discovery of principles underlying the behavior of the group, the value of the method will depend primarily on experimental demonstration of a certain degree of uniformity in the results obtained. In contradistinction to the practical applicability of a given method, therefore, its usefulness in scientific investigation will depend on the discovery of some common factors occurring in different members of the group, the actual existence of which can be demonstrated experimentally.

Of the methods that have recently been introduced in the study of mental diseases, few have been the cause of as much discussion and controversy on this particular point as that of the analysis and interpre-

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tation of dreams. In fact, the central question in this controversy is whether one is justified in building up generally applicable theories on the basis of data obtained by a procedure that so far has been shown to be of only practical value. It is true that in the latter capacity the dream has been shown to be of distinct value in practical psychiatry. Even if some of the more enthusiastic exponents are inclined to overrate the power of interpretation of dreams as an "open sesame" to all conflicts in human beings, most unprejudiced observers will not deny its value as an aid in understanding the mechanisms and in the treatment for mental diseases. The literature that has gradually accumulated on the subject shows that, empirically, the dream frequently affords definite indications of the conflicts instrumental in the development of mental disturbances, thereby pointing out a method of approach for their treatment.

The argument advanced by those who are interested in the scientific investigation of mental diseases, however, is that so far few successful attempts have been made to demonstrate experimentally the validity of analysis of dreams as a scientific method. It is true that some progress has been made in this direction, but in the cases of most investigators the work has not been carried to completion. As has already been suggested, an investigation of this type would not end with the empiric discovery of factors uniformly occurring in all dreams, but would go on to attempt to reproduce them experimentally. The discovery of such factors is of the greatest importance as it gives the elements out of which the question that one asks in the experiment is constructed. Usually it is in the practical work with individual patients that these observations are first made, and in the study of dreams the psychoanalytic theory was the first to point out the existence of such factors. The groundwork of the experiment thus being available, we thought that it would be of value to carry it on to completion. In the present communication, then, we shall present the results of experimental investigations undertaken with the purpose of finding out whether these factors can be demonstrated experimentally. As these observations form the central feature of the psychoanalytic theory of dream psychology, it is advisable to undertake a brief review of this theory before we proceed with a report of our procedure and the results. It is, of course, neither within the scope nor the purpose of this paper to give a complete presentation of this theory; for this we refer to the vast literature on this subject.[1] We shall restrict ourselves to a mere sketch that will serve the purpose of bringing out the factors that we are investigating and their relationship to the dream formation.

1. Freud, S.: Die Traumdeutung, Vienna, F. Deuticke, 1922. Vorlesungen zur Einführung in die Psychoanalyse, Internat. J. Psycho-Analysis **2**:238, 1922.

The psychoanalytic theory regards the dream as representative of a more or less disguised fulfilment of a wish that is otherwise repressed and does not gain access to the consciousness of the person when awake. This wish, which at one time has been actually experienced but not gratified, remains as a latent force in the subconscious level and reappears in the dream only when stimulated by a suitable recent occurrence. Thus, the wish appearing in the dream is associated with two actual experiences in the life of the person: (1) the original experience, which usually occurs in early life and forms the general background of the dream. Some time during the childhood or infancy of a person, a strong instinctive desire is prevented from being gratified by the fact that it comes in conflict with the other interests of the person (usually his adjustment to conventional society or family regimen). The fulfilment of such a wish or even the conscious thought of such fulfilment becomes associated with a feeling of guilt and fear of punishment by environmental forces. Because of this, the whole incident is repressed or forgotten, the wish itself remaining in the personality of the individual as a vague tension outside the conscious mind. The person does not willingly think of it, and actively resists the conscious recognition of any new experience that may bring the repressed factor into the sphere of consciousness. So that whenever the person comes into contact with any content in his environment that is closely associated with the original experience, he will tend to forget it too, thus letting the early repressed factor drag the recent experience out of the sphere of consciousness. This new experience, however, is not endowed with as much repressing force as the original one and is nearer to the conscious mind of the person. During sleep, this factor gains entrance to the dream and brings up with it in a disguised form the old incident which is now relived but with the difference that the wish is gratified. Thus we have (2) the recent experience with which the wish in the dream is usually associated.

These contents, that is, the wish and the two experiences associated with it, are regarded by the psychoanalytic theory as always occurring in dreams. In fact, in practical work the analysis of a dream is not considered complete unless both of these experiences are brought to light. It is easy to conceive why, practically, one would insist on discovering both experiences. For, as psychoanalysis regards the repressed wish as the central point of the conflict that causes the disease, the most logical way of reaching it is by uncovering both of these experiences and then searching for that content which is common to both. These factors, then, that have been found to occur regularly in all dreams are not only of didactic value as the basis for experimental investigation, but are practically of great importance, provided the truth of the assertion made can be objectively demonstrated.

In an investigation of this type one cannot but touch on another important psychopathologic problem to which psychoanalysis has brought a new aspect, namely, that of retention memory. According to the theory as we have outlined it, certain contents in a person's recent experiences, if they happen to be directly related to a repressed and painful incident, will also be repressed out of the field of consciousness. If the person in question is asked to describe those experiences, he will omit some of the contents, and one speaks of these as not having been noticed, or, if noticed, forgotten. But if some of these contents should afterward recur in the dream and be shown to be related to some previously repressed factors, one will be in a position to understand the mechanisms that cause such forgetting or not noticing. In other words, one will find that in case of at least some of these omitted factors, one is not dealing with simple, accidental lapses of retention memory, but with definite active repression.

In our experiments, therefore, we are to deal with the following problems: 1. Is it true that contents in our recent experiences that are forgotten are actually merely repressed and can be shown to recur in our dreams? 2. Do these contents bear a definite relationship to earlier incidents that have been repressed because of their conflicting tendencies? 3. Do both these experiences as uncovered in the analysis of dreams bear definite relationship to the life problems of the person and, in disease, to the conflict that is instrumental in causing the disease process?

For the purpose of answering these queries, we have employed the following procedure and material.

PROCEDURE AND MATERIAL

The procedure followed in this investigation was suggested by an experiment reported by Poetzl in 1918 [2] in the course of an investigation of indirect vision. Pictures of a presumably indifferent type were exhibited tachistoscopically to several normal persons. The pictures were exposed to the subjects for 0.1 second, following which the subjects were asked to describe what they saw. They had never seen the pictures before and were not aware of the nature of the experiment. After the description of the picture (a description that was naturally incomplete and sketchy), they were told that if they had any dreams that night they were to commit these to memory and relate them to the investigator on the next day. When these were reported, free associations of some of the dream contents were undertaken. The results as reported by Poetzl were striking in that the subjects in the dreams and especially in their associations brought out a surprising number of details of the pictures exposed that were not mentioned in the descriptions. A somewhat similar experiment was undertaken by Allers and

2. Poetzl, O.: Ueber experimentell erregte Traumbilder, Ztschr. f. d. ges. Neurol. u. Psychiat. **37**:278, 1918.

Teller in 1924.[3] These authors exposed the pictures for 0.04 second, and instead of dreams they used free and controlled associations after the descriptions of the pictures. Here, too, a great many of the factors that were omitted by the subject came out in the associations. As the procedure employed in the present investigation differed in some respects from that used by the authors named, we have restricted ourselves to a brief description of these, and thought it advisable to record in more detail the one used by us.

The subject is taken to a quiet, uniformly illuminated room, and is placed at a table with the examiner seated opposite him. The examiner first engages the subject in a conversation on some indifferent topic for about five minutes. The subject is then told that he will be shown a picture for a short period of time, and that he is to observe it well so that he can describe it with as many details as possible after the picture is removed. The picture is then placed on the table in front of the subject and is left there for thirty seconds. The picture is removed, and the conversation, interrupted by the exposure of the picture, is resumed again and continued for about five more minutes. After this the subject is asked to describe the picture in his own words, and is permitted to take as much time as he finds necessary in doing so. When he is apparently through with all the material he remembers, the subject is asked whether he could not think of anything else that was in the picture, and if more material is brought out, the question is repeated until the subject states definitely that he knows of no more. The descriptions are recorded verbatim along with the examiner's questions. The examiner, having studied these pictures before, subsequently analyzes the descriptions given by the patients with special reference to deviations from the actual details in the picture. It was found that most patients in their descriptions not only omit some of the details that were in the picture, but also add features that were not there. The analysis of the description then brings out two factors of importance—details omitted and details added. When the description is completed, the subject is told that if he should have any dreams during the night he should try to remember them, preferably write them down on awakening, and give them to the examiner the next day. These dreams are then recorded along with the description of the pictures.

In a few of the cases, free associations were attempted on some contents of the dream. In some cases, too, a second description of the picture was obtained on the second day when the patient was interviewed for the purpose of getting the dream. Usually only one experiment was carried out with each subject, but in some cases one or two additional pictures were shown, and the procedure carried out in the same way as with the first picture. The pictures used were of two types: (1) a series of copies of paintings in the Louvre museum that were not known to the patients, and (2) copies of paintings by Cezanne as reproduced in the book by J. Meier—Graefe on Cezanne. There was some selection of the pictures with a view to the possible relationship that they might bear to the conflicts in the particular case. Of the five pictures that are reproduced in the text, the first (fig. 1) was used in the case of practically all of the male patients. This was done primarily for the purpose of obtaining uniform results, but also because of the possibility of its being associated with infantile maternal attachments. All subjects were patients at the Psychopathic Hospital (with the exception of those in cases 1 and 2, who were patients at the Foxboro State Hospital[4]). The

3. Allers, R., and Teller, J.: Ueber die Verwertung unbemerkter Eindrücke bei Assoziationen, Ztschr. f. d. ges. Neurol. u. Psychiat. **89**:492, 1924.

4. Dr. R. B. Dexter, superintendent of the Foxboro State Hospital, gave us permission to use this material.

diagnosis in the different cases varied, but they were mostly psychoneuroses, affect disorders and schizophrenias. In all of these cases, analyses of varying degrees of depth were undertaken either prior to the experiment or following it. The information thus obtained gave us a good opportunity of judging the relationship between our experimental data and the actual life problems of the subject. The experiment was attempted in forty-seven patients (twenty-seven male and twenty female). For reasons that we are about to discuss, however, the attempts did not meet with the same degree of success in all cases.

From the description of the procedure used, it can be seen that it differed from that employed in Poetzl's experiment in two important points: 1. The pictures were exposed for thirty seconds instead of 0.01 second. 2. All of the subjects used were patients suffering with some form of mental disease instead of the normal persons used by Poetzl.

Both these changes were made in the interests of the special problems that we have undertaken to investigate. In making the first of the two changes we were guided by the fact that we were interested in the question of how true it is that impressions in everyday life may be repressed, afterward to be utilized in stimulating dreams. The tachistoscopic exposition of a picture for 0.01 second may cause a definite impression, but the descriptions of these pictures by the subjects show that this impression is not consciously clearcut and definite. In contrast to this, a picture observed for thirty seconds affords an experience that makes a definite impression, and is woven into the rest of the experiences of the day. In our own experiments this was shown to be true by the fact that practically all of the subjects retained their interest in the whole incident for a long time, remembering the picture well, although the characteristic deviations in its description became more accentuated. In fact, in the case of some of our schizophrenic patients, attempts were made to weave even the picture into their special delusional systems. The period of thirty seconds was taken arbitrarily, simply because we wanted to have a uniform length of time. In some cases the fact that the time permitted was so long brought remarkably good descriptions, with the observation of data that had previously eluded the notice of the examiners, and consequently leaving few if any omissions. This, of course, meant that there was not so much chance for the recurrence of such data in the dream; but we felt justified in doing this because only in this way could we be certain of reproducing actual life situations.

In making the second change in the procedure, we had in mind the problem that was presented in the third question outlined. It was clear that if we were to find out how much of a relationship there was between the omitted or added details, as well as the contents occurring in the dream and the conflicts of the subjects, a more or less complete analysis of the personality of the subjects would have to be available. Furthermore, these conflicts would have to be shown to be of great importance in determining the behavior of the subjects. But it goes without saying that in the case of normal persons this is next to impossible, no matter with how much of the person's life history one may be acquainted. With patients, however, in whom a special analysis was undertaken and the mechanism of whose mental disturbance was more or less definitely grasped, this was feasible.

The introduction of both of these changes was not without its disadvantages. In the first place, as was previously suggested, the long time of exposure permitted such complete descriptions that in some cases very little, and in some cases no, distortion occurred. This meant that we could not expect any positive results in the dreams. The use of psychopathologic cases caused further difficulties. Thus, for instance, some of the patients of a suspicious and paranoid type merely

kept back the descriptions of details, more or less as a matter of habit, usually being vague and indefinite in their productions. Other patients gave no account of dreams, some of them stating that they did not feel like talking about them, others again hiding behind the statement of not having had any (and there was no way of discovering whether this was true). In some of the patients, furthermore, the dreams were so completely mixed up with allusions to the particular difficulties of the patient in question that it was impossible to pick the dream contents from fantasy. Finally, another source of failure must be mentioned, one, however, that is not necessarily restricted to patients with mental disease. This difficulty arose from the fact that the exposition of the picture was after all only one occurrence in a whole day's event. During the course of the day there was always the possibility that something else that may have had a much closer association with this patient's particular repression would impress itself on the perception of the patient. These incidents would overshadow the contents of the picture in importance, and thus would interfere with the appearance of the latter in the dream.

RESULTS AND COMMENTS

Because of the type of material used and the procedure employed, the difficulties encountered in our experiment have reduced materially the number of cases in which definite, objectively valid results were obtained. Not wishing to encumber the report with the rather indefinite and highly speculative relationships that were found in a large number of our cases, we shall restrict ourselves in this report to data in which such relationships were clear and objectively evident. Furthermore, as this report is not primarily interested in the clinical aspect of the study of the cases, it was also thought best to confine ourselves, in most cases, to brief sketches of the results obtained in the analyses of the patients. It must be stated, however, that the relationships that were found to exist between the mechanisms of the development of the disease and the data obtained in our experiments were in most cases so strikingly evident that one was tempted to go into details even at the expense of brevity. We have, therefore, decided to compromise by giving a comparatively more detailed history of a few of the cases and restricting ourselves to brief sketches in the rest.

REPORT OF CASES

CASE 1.—C. S., a man, aged 34, married, whose case was diagnosed as psychasthenia, had a family history which showed a heavily tainted heredity and unfavorable home environment (alcohol, loose sexual morals, stealing, psychoses, etc.). A complete analysis undertaken in this patient brought out, among others, the following factors: Early in life an extreme attachment to the mother was developed and was associated with a reaction to the father consisting of a mixture of fear and hatred on the one side and a tendency to emulate him on the other. So far as could be seen, these reactions dated back to early psychic traumas due to parental indiscretions. Throughout the early life of the patient there were numerous signs pointing to his tendency to mold his own activities along those of the father and form heterosexual attachments toward members of the opposite sex that clearly represented the mother to him. His marriage, at the age of 33,

to a woman who was distinctly associated with the mother image was unsatisfactory, with a resulting development of neurotic manifestations. One month before the wife was to give birth to an infant, the patient developed a fear of appendicitis and, following this, obsessive ideas of mutilating himself. This was accompanied by dream states in which he saw himself persecuted and attacked by a man whom he associated with his father.

The picture shown was that of La Vierge au Coussin Vert (fig. 1). In his description the patient gave a surprisingly good account of the different details about the mother and child, as well as the background. He stated, however, that the child was looking away from the mother and had its left hand on the mother's breast as if pushing her away. Next day, the patient reported the following dream: He was sick and in bed. He wanted to eat and called for the nurse. The door opened and a lady dressed in dark clothes came in carrying a white bowl that he assumed contained soup. As she began to approach him he felt himself shrinking, becoming smaller, until he was the size of a small child. The

Fig. 1.—La Vierge au Coussin Vert, by Solario. (From a painting in the Louvre Museum, Paris; photograph by A. Bourdier, Versailles, France.)

nurse bent over him, and putting her hand under his head, pulled him up toward her, and with the other hand began to feed him from the bowl. To his surprise the material in the bowl was milk. On free association the patient associated the woman in black with his mother.

Here, then, the patient completely omitted describing the act of nursing. This afterward recurred in the dream in the form of his own regression to childhood, in which he is fed milk by the mother-nurse. The relationship of this to the patient's conflicts is clear. The picture apparently suggested his attachment to the mother and the wish for a repetition of early experiences. These had always been repressed, and the content of the picture that clearly tended to bring up this repressed factor was omitted from the description. In the dream both of them are combined around the background of the early repressed wish.

CASE 2.—M. M., an Italian woman, aged 34, married, in whose case the diagnosis was schizophrenia, had been brought up in a strict Catholic home environment in Italy. At the age of 16, she had a love affair which she now considered as sinful. It was not approved by the parents, and the patient had to break her relationship with this man. Shortly after this, the patient was in a boat with a young brother (7 years of age) who was left in her charge. The boat capsized, apparently through no fault of the patient, and the boy was drowned. The patient considered this a punishment for her sexual delinquencies and blamed herself for the death of the brother. Some time after that, she married a man considerably older than herself, for whom she had no affection. Her married life was not satisfactory. There were three children, and a few months before development of the patient's disease, the youngest of these, an infant, died of some infectious disease. In reaction to this the patient developed a depression, and conceived the idea that it was a punishment in retribution for her being the

Fig. 2.—Immaculate Conception, by Murillo. (From a painting in the Louvre Museum, Paris; photograph by A. Bourdier, Versailles, France.)

cause of her brother's death. This idea was the groundwork on which a delusional system of a schizophrenic type had developed.

The patient was shown the picture of the Immaculate Conception (fig. 2). In her description she referred to the figure as the Madonna. She described in detail the moon, the stars and the dress, but made no mention of the cherubs surrounding the Madonna. The next day the patient reported the following dream: She saw herself soaring to heaven and being surrounded by cherubs. Among them she recognized her brother and her own infant child. Curiously enough, following this dream she developed the delusion that her brother was really not dead, but was living somewhere away from her.

In this case, too, the relationships are brought out clearly. The psychosis was definitely precipitated by the loss of the infant child, which was associated with the feeling of guilt that she connected with the death of her brother. The picture of the Immaculate Conception

bringing up the disturbing factor is distorted in the description by the omission of the content that is associated with the feeling of guilt. In the dream these factors come up, and the cherubs assume the rôle of a fulfilment of the wish which is the central feature of the patient's psychosis.

CASE 3.—M. D., an American woman, aged 39, married, whose case was diagnosed as psychoneurosis, contracted a late marriage to an uninteresting man who was very much attached to his mother and who allowed the latter to rule the household. The patient resented this very much and felt that the mother usurped her place. Through the six years of married life the husband, at the advice of his mother, had used contraceptive measures, although the patient wanted children. With the appearance of signs of the menopause, a gradually increasing depression developed which culminated in an acute attack following a visit to a sister who was in a hospital recovering from an appendectomy. The patient associated the acute attack with seeing the amputated appendix in a jar at the sister's bedside. There was a mixture of depression and psychoneurotic symptoms from which the patient made a good recovery.

The picture shown was La Vierge (fig. 1). In the patient's description she gave a great many details of the background, but the mother and child were described poorly. She made no mention of the white head-cover, which was usually described by other patients, and was vague about the rest of the clothing. She added that she thought that the mother looked happy, stating immediately after that the examiner should not take that to mean that she associated this with her mother-in-law being happier than she was. She reported the following dreams the next day: She saw herself at home trying on a white wig before a mirror. She wished that she could look as well as her mother-in-law, who had white hair. Immediately after this, she saw herself in her home watching small pigs in water, and a goat ran after the patient. She grabbed it by the horns, but her mother-in-law came and took the goat away.

The patient's conflicts that apparently led to the development of the disease were clearly centered about her difficulties at home. The mother-in-law had not only taken the husband's affections from the patient, but had interfered with the fulfilment of a wish to have a child. All through the course of the disease she showed a pronounced hatred of the mother-in-law and a desire to possess that which the mother-in-law had, namely, a child and her husband. The association of the picture contents with her own condition was indicated in her remark following the description. The white head-cover, which was apparently associated with the mother-in-law's gray hair, is omitted in the description, and in the dream she finds herself wearing the white wig. It is possible too that the goat, the possession of which is disputed by the mother-in-law, is also symbolic of these difficulties.

CASE 4.—L. B., an American man, aged 28, married, whose case was diagnosed as depression (possibly conversion depression), had been brought up in a rather strict religious environment. There was a definite mother attachment in early life and a constant tendency toward competition with the father. This attachment to

the mother was subsequently transferred to a sister who was about one and one-half years younger than the patient. The sister resembled the mother very much, both being of very dark complexion and pyknotic type of physique. At school the patient had little to do with any of the children, associating only with his own sister. From the age of 11 to 13, there was a great deal of sexually colored play with the sister. This culminated in an unsuccessful assault by the patient on the sister at the age of 13. The sister threatened to tell the parents, and the patient was in a state of fear for the next two days. Following this an attack of what was diagnosed as encephalitis, with fever, nausea, headache, etc., developed. He considered this as a punishment for his activities with the sister. After recovery he began to practice auto-erotism with fantasies about the sister. Several attempts were made later on to form attachments of a heterosexual nature with girls who were definitely associated with the mother image, but in all of these cases attempts at intimate relations were followed by attacks of depression, headaches, nausea, etc. He regarded these as repetitions of the prodromal encephalitic symptoms. This patient finally married a person who was physically the direct opposite of both the sister and the mother, being blonde and of a slender, asthenic make-up. Directly after the marriage a series of depressions developed, followed by attempts at suicide, and the patient was brought to the hospital. Following the analysis, the patient made a good recovery.

The patient was shown the picture of La Vierge (fig. 1). The first description was one of great detail in which practically no factors were omitted, although the mother was described as being blonde. This was followed by a dream apparently having nothing in common with the picture. A second description obtained from him on the next day showed the following change: The child was lying in its mother's arms. It looked as if it were hungry, and the mother was about to nurse it. The mother was fair and looked like his wife. The next day he reported the following dream: He was in the hall of the hospital, and the nurse was with him. The nurse had her arms around the patient's neck and kissed him. She reminded him of his wife, although she looked as she did naturally, that is, of dark complexion and pyknotic make-up. Next they were both in his room lying in his bed. She had her arms around him, and he was kissing her on the face and breast.

In both experiments, then, the mother in the picture is described as being blonde, and in the second description the act of nursing is omitted. In the dream the woman is changed into a person who looks like the mother and sister, and the nursing is probably represented in the attitudes assumed by both the patient and nurse. Here again then the contents of the picture that are associated with the early incidents are omitted and reappear in the dream in the form of a fulfilled wish.

Case 5.—L. O., a white, American man, aged 26, single, in whose case the diagnosis was manic-depressive depression, had a heredity that was heavily tainted with manic-depressive psychoses and psychopathies. The father died when the patient was very young, and the patient has always shown a pronounced attachment to the mother. The attitude to the stepfather was one of dislike and contempt. The patient had a successful career at college, excelling especially in athletics. Sexually, he had shown a strong drive with sadistic tendencies. He had gone through a series of manic and depressed phases, his sexual drive being particularly strong in the manic episodes, whereas during the depressions he was rather prudish and penitent.

The first picture shown to this patient was "Murder" (fig. 3). The description was adequate, but with the following deviations: The sex of the person on the ground was given as male. There was no mention of the dagger in the man's hand, nor of the loose shirt shown in the picture. The sloping foreground of the picture was not described. Following this the patient had several dreams, the important factors of which were as follows: The patient saw a woman in a taxi that was driven by a Negro driver who intended to hurt the woman. The patient ran after the taxi in an attempt to help the woman. In another dream, the patient was in a dance hall. He saw a man (whom he identified as a movie actor who was at one time worshipped by the patient) dancing with a woman. The shirt-tail of the man was showing below his dress coat. Next he saw this man crossing the hall holding his phallus in his hand. In a third dream, he saw himself in a room that was divided in the center by a gully. He was on one side of it, and on the other there was a bed in which a figure was lying. The patient recognized in this figure a girl whom he had known some time before. He

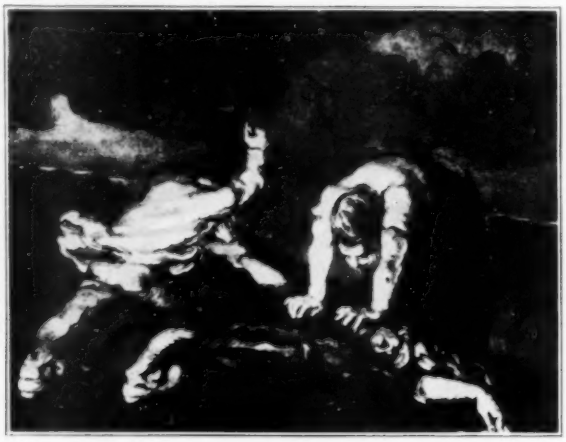

Fig. 3.—Murder, by Cezanne. (From the book on Cezanne by Julius Meier-Graefe, published by Ernest Benn, Ltd., London; Charles Scribner's Sons, New York.)

plunged across to the bed. The woman was frightened, and said that there was some one outside, whereon the patient awoke.

Some time after this experiment the picture of La Vierge (fig. 1) was shown to this patient. The details omitted here were the fact that the baby was naked and the description of the mother's clothes. The dream reported by the patient was as follows: His cousin Tom was in the house, and he was winding yards of yarn about the lower part of the body of a naked boy. He then saw himself in front of the church in which he was baptized. He saw two girls inside, and suggested a rendezvous to one of them. As he walked into the church, the preacher said: "There is a lady here to see you." On the door he saw his mother's coat.

In the first experiment the figure on the ground, which was usually described by other patients as a woman (because of the long hair), was described as a man by the patient. The knife and loose shirt-tail, as

well as the sloping foreground, are omitted. In the dream that starts out as an attempted assault, the victim is a woman. The change of scene shifts the active rôle from the Negro taxi driver to a movie actor whom the patient has always identified himself with and the connection with the picture is shown by the reappearance of the shirt-tail and, possibly, the symbolic representation of the knife in the form of the phallus. Finally, the dream ends with the patient in the active rôle, and the attack taking place across the sloping foreground of the gully. The patient had repeatedly stated during the analysis that his difficulties were all caused by his promiscuity and discrepancies. The contents of the picture, such as the woman being attacked and the sadistic nature of the attitude of the attacking man, are omitted in the description, but are clearly woven into the dream contents and built around the repressed wishes of the patient. In the second experiment, the association of the picture with the patient's early attachment to the mother causes the omission of details that are clearly recognized in the dream following it.

Case 6.—C. P., a white American woman, aged 48, divorced, whose case was diagnosed as a reactive depression following the prolonged use of drugs, had always had difficulties in adjustment. Following the severance of an unsatisfactory marital situation, she became addicted to alcohol and the use of narcotics. This brought about the occurrence of periodic depression and an exaggeration of a previously inadequate personality. She began to make exacting demands on her children (son and daughter) and to accuse them of disinterestedness and lack of affection (some of which was not altogether without foundation). These traits had become especially pronounced within the last three years and culminated in a definite depression and attempt at suicide that brought her to the hospital.

This patient was shown the picture of the Immaculate Conception (fig. 2) which she described very well, but with the following deviations: The faces of the cherubs were described as being turned away from the Madonna and the crescent under the Madonna's feet was not mentioned. This was followed by a dream in which the patient saw herself with her son sitting at her feet and looking up to her with an expression of affection. He was telling her that he was selling planetariums and showed her some of the constituents such as the moon and the stars.

The patient who had gone through a difficult marital situation had placed all her hopes for compensation on the children. Her depression is clearly centered about the disappointment in this and the grievances, both real and imagined, against the children. The adoration and affection for the mother expressed in the upturned faces of the cherubs, as well as the crescent under the Madonna's feet expressive of her exalted position were associated with all that the patient secretly desired and did not possess. They were omitted from the description and then recurred in the dream in the form of a fulfilled wish.

Case 7.—W. D., a white man, an American, aged 29, married, in whose case the diagnosis was conversion depression, was an intellectually dull person, of a sensitive make-up, who had grown up with a feeling of his own inadequacy, intellectu-

ally as well as sexually. His marriage to a woman who considered herself superior to him (an attitude which the patient felt was justified) helped in increasing this sense of inferiority. Following an injury to one testicle and an operation for hydrocele on the other, the patient began to develop the idea that his wife was going to leave him because of his sexual inadequacy, and was going to take their children away with her. He became depressed, and, following some minor legal entanglements, the seriousness of which his acquaintances exaggerated, playing on his credulousness, a state of pronounced apprehension and anxiety developed. He spoke of the police being after him, that he was going to be murdered, the children were to be tortured, etc. It was in this state that he was brought to the hospital.

The patient was shown the picture of Medea (fig. 4). (This picture represents Medea who is about to murder the children that she bore to Jason in revenge for

Fig. 4.—Medea, by Cezanne. (From the book on Cezanne by Julius Meier-Graefe, published by Ernest Benn, Ltd., London; Charles Scribner's Sons, New York.)

the latter's infidelity to her.) He described the picture as that of a man, and did not mention either the children or the dagger. The apparently distorted condition of the left forearm was also left out. The dream obtained from him the next day was not very clearly related: "Something was the matter with my arm (pointing to the left arm). All the meat came off (pointing to the muscles of the forearm) so that I could see the bone. I had a baby in this arm (the right). Everything else was not clear. I thought my wife was there and gave me a baby."

The difficulties that precipitated the mental disturbance in this case were especially centered about the wife of the patient, his fear of injury to himself or his children, and his inferiority accentuated by the operation. The details omitted in the description of the picture seem to be

closely associated with these difficulties. The knife and the children are altogether left out, and Medea is described as a man. In the dream the patient is in possession of one of the children and the other is being given back to him by his wife.

CASE 8.—J. W., a white man, an American, aged 28, married, whose case was diagnosed as a psychoneurosis, had always been much attached to his mother and dependent on her. Early experiences led to a linking up of this feeling, which had a definite sexual element in it, with that of fear and guilt. During adolescence, he went through a great number of superficial attachments. Shortly before admission, he married a girl who evidently represented the mother to him. Directly after the marriage, the patient discovered that he had made a mistake, left his wife, and subsequently a depression developed. There was no attempt made at marital relations, and the analysis revealed that the patient's reaction was due to a feeling of sexual inadequacy connected with an attitude of fear and guilt toward the marital situation.

He was shown the picture of La Vierge (fig. 1). In his description he mentioned no details of the child, merely stating that it was there. The same was true of the mother. The background was described in great detail. In his dream he first saw himself on a dark street. A woman "whose face he could not see well but who was dressed in a wide kimona" gave birth to a child right on the street. This child "was very large, looked about a year old, had curly hair," and the patient went on, describing the child in the picture. Some people on the street were laughing, and asking whose child it was. This dream faded into the next one in which the patient found himself with his mother. She was imploring him to come back, telling him not to have any fear and that "everything will be all right now."

The details omitted in the description come out strikingly in the dream. The relationship between these details omitted and the problems of the patient is also clearly indicated in the dream, even if an attempt is made to disguise it. An interesting factor, frequently pointed out by Freud, is the shifting of the scene by splitting the dream into two parts to help in making the transition from a person unknown to the one known (the mother).

CASE 9.—D. E., a white, American woman, aged 24, single, whose case was diagnosed as schizophrenia, had homosexual fixation on the mother, which was transferred to a neighbor after the mother's death and finally to a middle aged female employee at a sanitarium, and led to the development of a paranoid system. In this system the patient spoke of these persons as persecuting her, watching her and trying to force their affection on her. She was shown the picture of Mme. Le Brun and daughter (fig. 5). In her description the patient did not emphasize the pronounced difference in the age of the two figures and thought that they were sisters, adding that the picture was to represent "sisterly love." No mention was made of the fact that the person standing had her arms around the other's neck. In the dream reported by her she saw the neighbor (who was previously mentioned) who was trying to watch her by a series of mirrors and act on her with electricity.

In this experiment, too, therefore, the factor in the picture (i. e., the mother-daughter relationship and the active clinging of the daughter to the mother), which were indicative of the patient's own attachment to her mother, were not mentioned. In the dream, the mother substitute reappeared, taking the place of the sister in the patient's description. A somewhat similar situation is seen in the next case.

Case 10.—M. H., a white, American woman, aged 19, single, whose case was diagnosed as a psychoneurosis, had grown up under the exaggerated protective attitude of the mother, on whom she had always been very dependent. The picture shown to this patient was the same as that in case 9 (fig. 5). The patient mentioned that the mother had her arms around the daughter, but omitted the description of the girl's arms being about the mother's neck. In her dream she saw herself with her older sister, with her arms about the sister.

Fig. 5.—Portrait of Mme. Le Brun and Daughter. (From a painting in the Louvre Museum, Paris; photograph by A. Bourdier, Versailles, France.)

Case 11.—S. F., an American woman, white, aged 42, married, whose case was diagnosed as a paranoid state, was of a sensitive, suspicious make-up with a pronounced feeling of inferiority. The sense of sexual inadequacy and the suspicion that the husband was not satisfied with her led to the development of projections in which she imagined that the husband was forcing her to be intimate with another man. The picture shown to this patient was that of "Olympia" by Cezanne. In this picture the artist has probably reproduced the scene in which Olympia, the wife of Philip of Macedonia, is captured by Cassander. The three persons in the picture are Olympia, her maid and the man (probably Cassander). The patient interpreted the picture as applicable to her case "I've been captured myself for fifteen years" (meaning by the husband). She stated, however, that besides Olympia there were two men in the room and no mention was made of the maid. In her dream she saw herself in a situation more or less like the one in the picture, with the difference that she was with another woman and was trying to hide from a man who wanted to get into the room.

Both the description of the picture and the contents of the dream, then, are definitely related to each other and to the particular difficulties that have led to the development of the psychosis in this case.

In the analyses of the description of the pictures by the patients, it was interesting to note the relationship that was found to exist between the details added and the particular problems that the patients were facing at the time. These were usually accompanied by subjective interpretations. Some of these have already been mentioned in the cases quoted. Thus in case 1, we find the patient describing the child as actually "pushing the mother away." This was probably conditioned by the life-long struggle of the patient against his attachment to the mother. In case 3, the added detail that the mother looked happy, further qualified by the reference to the mother-in-law, clearly indicated the feelings that were the central feature of the patient's difficulty, namely, the idea of happiness as associated with motherhood and the envy of the mother-in-law. In case 4, the patient in his second description, after omitting to mention that the child was nursing, added the statement that the "child was hungry and looked as if it wanted to nurse." From the analysis of this case it seemed logical to assume that this was indicative of the failure on the part of the patient to emancipate himself completely from the desire to relive the infantile situation. Similar indications were found in a number of other cases, as for instance:

CASE 12.—C. V., a white, American man, aged 30, single, whose case was diagnosed as schizophrenia, was an effeminate man, who had always shown female characteristics in his voice, mannerisms, dress and sexual prudishness. He was shown the picture of La Vierge (fig. 1). He described it well, but stated that the child was a girl and had a dress on.

CASE 13.—H. T., a white, American man, aged 38, single, whose case was diagnosed as dementia paralytica, while in the hospital had acquired a pronounced attachment to the nurse in charge of the ward (the only woman in a white uniform on the ward). He was shown the picture of La Vierge (fig. 1). He described the mother as having on a white dress and white shoes and stockings.

CASE 14.—F. C., a white, American man, aged 58, married, whose case was diagnosed as an agitated depression (involutional), had suffered some financial losses and went into a state of depression. This condition had gradually developed into a deep agitated depression with somatic delusions. He conceived the idea that he had always had some "very bad blood disease," and that he was finally suffering the effects of it. This patient was shown La Vierge (fig. 1). His description was rather inadequate and interspersed with subjective interpretation. One remark was of especial interest: "I can see the disease flowing from one to the other. The child is draining the poison from the mother."

CASE 15.—R. S., a white, American boy, aged 13, single, whose case was diagnosed as a behavior problem without definite signs of mental disease, because of a pronounced precocity in physical development, had always appeared much older than he actually was, and to a certain extent felt himself forced to behave accordingly. This brought about difficulties in adjustment at his real level. On

several occasions he ran away from home and while away he always succeeded in playing the part of an adult. The picture shown to him was that of La Vierge (fig. 1). He was vague in his description of the child, stating that it looked like 2 years old, and omitting the fact that it was nursing.

It would seem as if the patient in case 15 had transferred his own tendency to appear more mature than he actually is into the description of the picture. A similar tendency to subjective coloring could also be seen in the following case:

CASE 16.—E. H., a white, American woman, aged 31, married, whose case was diagnosed as schizophrenia, as the result of a difficult marital and social situation suffered an acute psychosis. She conceived the idea of being sinful, wanting to harm her husband and children, etc. The picture shown to her was that of Medea (fig. 4). In her description she said: "It was a man in doubt just as if he did not know what to do. . . . Maybe he had already killed his wife."

CONCLUSIONS

The results reported show primarily that analysis of dreams, at least that phase of it that we have investigated, can be used as a method in scientific research. We feel justified in making this statement, because we found that: (1) the factors regarded by the psychoanalytic theory as uniformly occurring in dreams were demonstrated in the dreams of a number of our patients, and (2) they could be experimentally induced.

In reference to the questions that, in our introduction, were taken as the basis of the present experiment, these results permit the following answers: 1. Some contents in the recent experiences of our subjects that were left out of their descriptions were subsequently shown to recur in their dreams. 2. These contents seemed to have a definite relationship to experiences in the earlier life of the person. 3. Both of these experiences were found to be definitely related to those problems in the subjects' lives that, as far as could be judged, formed the central feature of the disease process.

It must be remembered, of course, that in coming to these conclusions we have considered only the cases that were reported, that is, only a part of the subjects that were used in the experiment. In our description of the procedure, we have discussed the difficulties that could be regarded as causative of the lack of success in a large proportion of our cases. In most of these the explanation was adequate and could not be taken as contradictory to the preceding conclusions. Thus, for instance, a perfect description of the picture without the omission of any details, so far as we could judge, could only suggest that there was nothing in the contents of the picture that was related to the patients' problems. The absence of relationship between the subsequent dream and the picture, therefore, would have no bearing on our problem. Then

again, the refusal on the part of the patient either to describe the picture or to relate the dreams must be regarded in the same light. This evaluation also applies to dreams forgotten or the statement that the subject had not dreamed. There was, however, a small number of cases in which some contents in the picture were not mentioned in the description, but nevertheless did not reappear in the dream. The explanation that has already been suggested, namely, that these patients may have had other experiences during the day that were more closely associated with their particular problems than the contents of the picture, and thus overshadowed the latter, is logical but, we admit, needs further proof. When we consider the fact that Poetzl in his experiment with normal persons and tachistoscopic exposition obtained the same results in all of his cases, we feel justified in assuming that most, if not all, of our unsuccessful attempts were due to the difference in material used and the procedure that was followed.

Outside of its value as an aid in the experimental investigation in which we were primarily interested, the procedure described can also be utilized in practical clinical as well as psychologic work. The comparative ease with which the conflicts, instrumental in the precipitation or even causation of the mental disturbance, can be brought to the surface in some cases by this procedure makes it particularly valuable in patients in whom these conflicts are deeply hidden under the surface. In the field of practical psychology, it seems to offer a new method of approach for the investigation of retention memory.

Above all, the results of this study emphasize once more a fact, so frequently pointed out within recent years, that no matter how irrelevant or accidental psychic phenomena may appear, they are actually closely related to the functions and problems of the whole personality.

THE NEURAL SYMPTOMS AND SIGNS IN PERNICIOUS ANEMIA

THE EFFECTS OF LIVER EXTRACT *

K. C. SMITHBURN, M.D.
AND
L. G. ZERFAS, M.D.
INDIANAPOLIS

Following the early descriptions of pernicious anemia by Combe,[1] Addison [2] and Biermer,[3] other investigators reported the occurrence of changes involving the nervous system in patients suffering with this disease. Lichtenstern [4] described certain lesions of the spinal cord, Hamilton and Nixon [5] reported symptoms which they ascribed to peripheral neuritis, and Woltman [6] called attention to involvement of the brain. The pathology of lesions of the central nervous system has been described by many investigators. There is also an abundance of literature on the clinical symptoms and signs with reference to the neural and psychic changes.

REVIEW OF THE LITERATURE

Numerous theories have been advanced regarding the etiology of pernicious anemia and the associated neural manifestations. Several British investigators, most notably Hurst,[7] have stated the belief that the predisposing factor is achylia, and that the anemia and subacute combined degeneration of the cord are caused by intestinal intoxication, which is a result of the achylia. Castle,[8] and Castle and Townsend [9] advanced evidence in favor of the hypothesis that pernicious

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anemia is a deficiency disease, the deficiency occurring in the gastric digestion of proteins. Means and Richardson [10] stated that "it would seem fair to assume, in view of the newer facts, that pernicious anemia is in some sense or other a deficiency disease." Meulengracht [11] called attention to possible hereditary factors in achylia, glossitis and pernicious anemia. Skoog [12] suggested the possibility that achylia, anemia and changes in the cord may be resultants of physiologic or pathologic changes in the vegetative nervous system. M'Gowan [13] stressed the point that overproduction of the organically deranged bone marrow plays a greater part in the disease than liver deficiency. Cornell [14] stated that pernicious anemia is probably a disorder of metabolism.

Much has been written regarding the neural symptoms and signs occurring in this disease, and their incidence has been variously quoted. Reese and Beigler [15] stated that 80 per cent of the patients with pernicious anemia have greater or lesser involvement of the nervous system, while Hurst [16] found neural manifestations in 85 per cent of the patients studied. Grinker [17] gave the incidence as 30 per cent, but included only cases with well defined, combined systemic disease. Reese and Beigler stated that impaired vibratory sense in the extremities is usually the earliest neural manifestation, while others have stated that paresthesia appears first. Numerous cases are on record in which paresthesia preceded the discovery of anemia by months or years (Cabot [18]).

In regard to the effects of liver therapy on the neural symptoms and signs, Minot and Murphy [19] stated that no great change occurred in the patients with pernicious anemia who had marked symptoms or signs due to degeneration of the spinal cord, although improvement was noted in the less severe neurologic phenomena. Ordway and Gor-

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ham [20] confirmed these observations. Sloan [21] reported improvement in the ataxia, while Robertson and Gowen,[22] Conner,[23] Ungley and Suzman,[24] and Bubert [25] reported even more marked improvement in the nervous and mental condition of patients following the administration of liver extract or of a diet rich in liver. Cohen,[26] Sturgis, Isaacs and Smith,[27] McAlpine [28] and others, however showed that lesions of the spinal cord may appear for the first time or may be progressive during liver therapy.

This report is based on a clinical study of 115 cases of pernicious anemia. Patients included in the series have been studied for periods varying from one to forty-three months, the average period of observation being eighteen and one-half months.

METHODS OF STUDY

All of the patients were treated with potent fractions of liver except three, who were given desiccated hog's stomach. Amounts of potent fractions of liver adequate to maintain a normal red blood cell level were employed except in a comparatively small group of patients who were given various daily amounts in order to determine the maintenance dosage. The following plan for routine study was adopted:

A detailed history and physical examination were obtained on the patient's admission to the hospital. Laboratory examinations included as a routine: urinalysis, examination of stools, gastric analysis, quantitative blood bilirubin determination, Wassermann test of the blood, and daily studies of the blood, including red cell, white cell and reticulocyte count and hemoglobin determination. A suitable control period was allowed, after which liver therapy was started. Following the reticulocyte response, the general condition permitting, the patient was released. Patients were requested to return for monthly examinations, and, although a few failed to cooperate in this respect, the majority of the patients adhered to the prescribed regimen. In the initial examinations and in the subsequent periodic reexaminations especial attention was directed toward the three principal systems involved in pernicious anemia, namely, the blood, nervous and gastro-intestinal systems.

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SYMPTOMS

The symptoms and signs referable to the neural system that we observed were: paresthesia, anesthesia, hyperesthesia, impaired sense of vibration, impaired muscle and bone sense (including position), impaired touch, pain and temperature sense, ataxia, altered tendon reflexes, altered cutaneous reflexes, loss of sphincteric control (retention or incontinence), girdle sensations and impaired equilibratory sense and mental symptoms including depression, irritability, slow thought or speech, hallucinations, illusions, disorientation, ideas of persecution, homicidal tendencies and flight of ideas.

Of all the neural symptoms, paresthesia was by far the most common; 110 of the 115 patients (95.6 per cent) complained of this condition. The toes and feet were first involved, then the fingers and hands, the numbness in a few instances progressing so that the lower extremities were numb up to the hips and the upper extremities to the

TABLE 1.—*The Incidence of Cases by Age and Sex*

	Age in Years						
	21 to 30	31 to 40	41 to 50	51 to 60	61 to 70	71 to 79	Totals
Male	3	1	11	26	17	6	64
Female	2	5	7	23	13	1	51
Total	5	6	18	49	30	7	115

shoulders, the trunk becoming involved last. The tingling sensations in most cases were less marked when the patient was at work.

In a few instances areas of complete anesthesia were found in various parts of the body. Hyperesthesia was more common and more often called to the attention of the examiner by the patient. Impaired sense of vibration over the long bones was present in a large percentage of cases. In a few of the patients in whom neurologic manifestations were pronounced, the loss of muscle and bone sense was so marked that the patient was unable to determine the position of the extremities without seeing them

Ataxia was seen in forty-eight cases, thirteen of which were probably due only to muscular weakness as other evidence of degeneration of the cord was absent. In this type of ataxia, marked improvement under liver treatment may be expected in direct proportion to the increase in muscular strength. Of the cases of ataxia due to involvement of the spinal cord, two types were seen: the flaccid type with obtunded tendon reflexes and steppage gait resembling tabes, and the spastic type with hyperactive reflexes.

Girdle sensations were present in a number of cases and were invariably the source of much discomfort to the patient. Abdominal crises occurred, but were not common, and, as Bailey [29] pointed out are not to be confused with surgical conditions of the abdomen. In making this differentiation, a white blood cell count, as well as an erythrocyte count, blood smear examination and neurologic study, are of value.

During a severe relapse of the anemia, mental symptoms were common, consisting of marked depression, introspection, irritability, slow thought or speech and impaired memory. Seven of the 115 patients (6 per cent) showed definite evidence of a psychosis, with hallucinations, illusions, flight of ideas, disorientation, delusions of persecution and homicidal tendencies. One of these patients was committed and is now in a hospital for mental diseases. Another died with a violent, maniacal form of mental disease.

Intercurrent infections attended by fever apparently caused rapid increase in the cord symptoms in a few cases. In one instance, a patient with only slight evidence of degeneration of the spinal cord suffered an attack of acute cholecystitis, following which the cord symptoms and signs were much more in evidence. Paresthesia, diminished vibratory sensation over the long bones and obtunded tendon reflexes developed during an attack of pyelitis and nephritis in a second patient, who on admission to the hospital, showed no neural symptoms or signs.

CHANGES IN NEURAL MANIFESTATIONS FOLLOWING LIVER THERAPY

Minot, Cohn and Lawson [30] reported the changes in the blood following adequate daily doses of liver extract, and stated that the active principle appears to cause a disappearance of, and to prevent the development or progress of, certain neural manifestations. In the series of cases here reported, there was, in a majority of instances, early improvement in the sensations of numbness and tingling. Many patients stated that the paresthesia had entirely disappeared. In other instances these sensations persisted, and in a few cases became more severe and more extensive. The latter was particularly true in the patients in whom the manifestations were already fairly extensive, and the history of whose illness extended over a period of several years.

The change in the mental attitude and condition was marked and occurred relatively early. The attitude of depression, dejection and negativism usually became one of elation, cheerfulness, optimism and cooperation in about two weeks corresponding in a general way to the

29. Bailey, H.: Brit. M. J. **2**:554 (Sept. 25) 1926.

30. Minot, G. R.; Cohn, E. J., and Lawson, H. A.: Am. J. M. Sc. **125**:599 (May) 1928.

response of the blood. However, in the type of patient who had a definite psychosis, the improvement, if any, was likely to be less striking and to require more time. In a few instances, ideas of persecution, hallucinations and illusions persisted over a period of many months without any evidence of change. In three instances, mental symptoms were progressive and apparently unaffected by liver extract in quantities adequate to maintain the normal erythrocyte level.

In many cases, ataxia improved early. This was particularly true when the ataxia was caused by muscular weakness. The patients with ataxia, hyperactive tendon reflexes and toe reversal signs were slow to improve, if improvement took place at all.

TABLE 2.—*The Number and Percentage of the More Outstanding Neural and Psychic Symptoms and Signs Observed in 115 Patients with Pernicious Anemia on Admission to the Hospital and at Subsequent Examinations*

Symptom or Sign	Number	Per Cent
Paresthesia	110	95.6
Ataxia	48	41.7
Impaired muscle and bone sense	39	33.9
Obtunded tendon reflexes	41	35.6
Exaggerated tendon reflexes	19	16.5
Muscle pains	49	42.6
Joint pains	16	13.9
Loss of sphincter control	8	6.9
Mental depression	59	51.3
Slow thought or speech	28	24.4
Loss of memory	11	29.5
Irritability	32	27.8
Introspection and self pity	26	22.6
Illusions or hallucinations	7	6.0
Disorientation	17	14.7
Ideas of persecution	10	8.6
Homicidal tendencies	3	2.6
Psychosis	7	6.0

We observed no change in the cutaneous or tendon reflexes while the patient was under treatment with liver extract, except that in several instances the reflexes that were inhibited were found later to be entirely absent, and when hyperactive to be more markedly so.

For purposes of more accurate observation, we selected patients with definite evidence of degeneration of the spinal cord or psychosis, or both, for special study. Thirty-five patients (30.4 per cent) had unmistakable combined systemic disease or psychosis and were placed in the "neurologic" group. Three of these patients had definite psychosis without marked evidence of combined degeneration of the spinal cord. Four others had definite psychosis and marked evidence of lesions in the spinal cord. The remaining twenty-eight patients had advanced combined systemic disease with few or no psychic symptoms. In this group of neurologic cases improvement was seen in paresthesia more frequently than in any other symptom or sign. The improvement in ataxia and sphincteric control (table 2), the relief of mental depression and improvement of

memory were apparently due to increased muscular strength and improvement in the general condition resulting from an adequate response of the blood.

The following cases are representative of those we classified as "neurologic" and illustrate both the improvement and retrograde changes that may occur during treatment of patients with pernicious anemia with potent fractions of liver.

REPORT OF CASES

CASE 1.—*Clinical History.*—H. McF., a white man, a farmer, was first seen at the Robert W. Long Hospital on June 27, 1927, when he complained of weakness, fatigue, soreness and tenderness over the entire body, epigastric pain and numbness and tingling in the extremities. The onset of the illness had occurred four and one-half years prior to admission and was characterized by abdominal pain and belching. Two years after this, he became pale and yellow, and began to notice numbness and tingling in the lower and then in the upper extremities. His memory for details was rather poor, but he stated that several times during the four and one-half years he was fairly well and able to work; then he became ill again. During the four and one-half years he had lost 38 pounds (17.2 Kg.) in weight. The past history and family history were without significance.

Physical Examination.—There were: icteric skin and sclerae; pallor of the mucosae; atrophic tongue; tender, palpable spleen; obtunded deep reflexes, and slight hyperesthesia over the extremities.

Laboratory Examination.—The Wassermann test of the blood was negative; the van den Bergh test gave a direct delayed positive reaction; gastric analysis revealed achlorhydria; the erythrocytes numbered 1,220,000 per cubic millimeter; leukocytes, 4,000 per cubic millimeter; hemoglobin, 34.1 per cent, and reticulocytes, 1.8 per cent. Examination of stained films of the blood showed a typical red cell picture of pernicious anemia in relapse.

Treatment and Course.—The patient was treated with a potent fraction of liver; a satisfactory rise in reticulocytes and erythrocytes and marked improvement in the general condition resulted. While in the hospital he suffered an attack of severe pain in the upper part of the abdomen, accompanied by nausea and vomiting. This was at first thought to be due to cholecystitis, but later was recognized as an abdominal crisis. The patient was released on August 25 in a much improved condition.

Following release from the hospital, he recovered sufficiently to return to farm work. In October, he worked for a week in a silo, and during the greater part of the time his feet were wet. At the end of the week, paresthesia was so extreme that he had to go to bed. He was readmitted to the Robert W. Long Hospital on November 7, complaining of weakness, inability to walk and extreme generalized soreness. The tendon reflexes were absent, and there was marked hyperesthesia of the entire cutaneous surfaces of the body. He was unable to stand. Muscle, tendon and joint senses were markedly disturbed. There was little coordination in the movements of the extremities. The erythrocyte count at this time was 4,300,000; the hemoglobin was 90.5 per cent. Liver extract treatment was continued, and the patient was able to walk with assistance when released on December 18.

Liver extract in amounts derived from 600 Gm. of fresh liver was taken daily until May 28, 1928, when the dose was decreased one-half. The patient continued to take daily the amount of extract derived from 300 Gm. of fresh liver. The erythrocyte count has remained normal, and the state of general health is good. He still complains of numbness below the knees and some difficulty in walking. The hyperesthesias have disappeared. The tendon reflexes are absent. He is able to do a full day's work on the farm each day.

Comment.—The points of greatest interest in this case are that the patient had what might be termed a recurrence of nervous symptoms while taking daily adequate doses of liver extract at a time when the erythrocyte level was practically normal; that, under continued administration of liver extract in large doses, there was marked improvement in coordination, ataxia and hyperesthesia, as well as in general physical strength.

TABLE 3.—*The Incidence in the Neurologic Group of the More Important Symptoms and Signs Together with the Number of Changes Noted After Liver Extract Therapy for an Average Period of Nineteen and One-Half months*

Symptoms or Sign	Number of Cases	Per Cent of Cases	Number Improved	Number Progressive	Number Unchanged
Paresthesia	35	100	18	10	7
Ataxia	33	94.3	7	9	17
Impaired muscle and bone sense	33	94.3	..	10	23
Exaggerated tendon reflexes	10	28.5	..	3	7
Obtunded tendon reflexes	21	60	..	7	14
Loss of sphincter control	8	22.8	2	6	..
Muscle and joint pains	21	60	7	8	6
Mental depression	22	62.8	7	9	6
Loss of memory	16	45.6	8	6	2
Flight of ideas	7	20	..	5	2
Hallucinations	5	14.2	..	5	..
Illusions	7	20	..	5	2
Ideas of persecution	7	20	..	5	2
Homicidal tendencies	3	8.5	..	3	..

CASE 2.—*Clinical History.*—L. J., a white man, aged 60, a machinist, was admitted to the Indianapolis City Hospital on Feb. 11, 1928, complaining of weakness, fatigue, dyspnea, palpitation, numbness and tingling in the extremities, intermittent diarrhea and constipation, loss of appetite, loss of the sense of taste, swelling of the ankles, sore mouth and tongue, jaundice, difficulty in expressing his thoughts, vertigo and irritability. The illness dated back about eighteen months, during which time he had had three transfusions of blood. He had also been treated with the Minot-Murphy liver diet, which he abandoned. One brother had had tuberculosis; otherwise the past and family history were unimportant.

Physical Examination.—The skin and conjunctivae were a pale lemon yellow; the tongue was red and atrophic; the gait was ataxic, and the tendon reflexes were exaggerated.

Laboratory Examinations.—The erythrocyte count was 2,270,000 per cubic millimeter; hemoglobin, 63.6 per cent; the leukocyte count, 6,900 per cubic millimeter. The urine was normal. A Wassermann test of the blood was negative. Gastric analysis revealed achylia. The blood bilirubin was 0.55 mg. per hundred cubic centimeters. Examination of blood smears showed many macrocytes well filled with hemoglobin, and 1.24 per cent reticulocytes.

Treatment and Course.—Starting on February 21, the patient was treated with liver extract no. 343 in daily amounts derived from 300 Gm. of fresh liver. The patient improved considerably and was released from the hospital on February 29. The response to treatment was not marked, but there was a gradual increase in the number of erythrocytes to 3,940,000 on July 7.

Second Admission.—The patient returned to the hospital on November 2, complaining of increased numbness of the hands and of the lower extremities up to the thighs, inability to coordinate movements, difficulty in walking, coldness in the extremities and inability to concentrate. There was slurring of speech and omission of words. He had at times become disoriented and threatening, and he had hallucinations and illusions.

Physical Examination and Course.—The results of examination were essentially the same as on the previous admission. Urinalysis revealed normal results. The erythrocyte count was 2,290,000 (he had failed to take liver during the month prior to admission) and increased to 3,400,000 before release from the hospital on December 15. There was some improvement in the general condition during the stay in the hospital, but no improvement in the neural and psychic disturbances.

Following release from the hospital, he continued to take daily the amount of liver extract derived from 300 Gm. of fresh liver, but the changes in the spinal cord and mental symptoms progressed to the point of complete ataxia, complete disorientation and a maniacal type of mental disease. Death occurred on June 10, 1929.

Comment.—The outstanding features in this case are the advanced lesions in the spinal cord, associated with a psychosis, both of which were progressive during treatment with liver extract.

Case 3.—*Clinical History.*—B. B., a white woman, aged 63, a housewife, was admitted to the Indianapolis City Hospital on July 11, 1929, complaining of numbness and tingling in the upper and lower extremities, precordial pain, dyspnea on exertion, inability to walk, sore mouth and tongue, loss of appetite, diarrhea, weakness and incontinence. The onset of the illness had occurred two months before admission. The first symptoms were numbness and tingling in the fingers and toes, followed by cramplike pains in the lower extremities, difficulty in walking and involuntary urination and defecation. Severe diarrhea also developed about this time, and the patient became very weak. She noticed some changes in the color of the skin, and she had lost the senses of taste and smell. The past and family history were irrelevant.

Physical Examination.—The skin was moderately bronzed, and the sclerae were icteric. The tongue was markedly atrophic and presented numerous furrows over its surface. There were marked dental caries. The tendon reflexes were exaggerated. There was considerable loss of muscle and bone sense (position) and almost complete loss of pain and temperature sense in the lower extremities.

Laboratory Examinations.—The erythrocyte count was 1,040,000 per cubic millimeter; hemoglobin, 27.4 per cent, and the leukocyte count, 2,500 per cubic millimeter. The van den Bergh test showed delayed positive reactions, the gastric analysis, achlorhydria and the urinalysis, a trace of albumin and many pus cells.

Treatment and Course.—The administration of liver extract no. 343 in daily amounts derived from 300 Gm. of fresh liver was started on July 25. The hematopoietic response was interrupted on August 4 by an acute attack of pyelitis which lasted for three weeks. Subsequently, the blood returned to normal. There

was gradual improvement in the neural symptoms, so that by the time the patient was released on November 2, she had regained control of the sphincters and was able to walk by supporting herself. The numbness of the extremities improved slightly. The tendon reflexes remained hyperactive. This patient remains in fairly good general health after more than a year, but is yet unable to walk unassisted.

Comment.— This case is one of apparently rapid onset, a rapidly progressive course, which was arrested by treatment, and of early extensive involvement of the neural system. A large part of the apparent neurologic improvement was probably due to improved general health and increased physical strength.

COMMENT

In studying a case of pernicious anemia in relapse, with associated mental symptoms, it is often difficult to determine at once whether the mental symptoms are due only to the low level of the blood or to a definite psychosis. However, we have found that when irritability, introspection and mental depression alone are present, the outlook for improved mental condition is good; when hallucinations, illusions, ideas of persecution and homicidal tendencies are present, the prognosis for recovery of mental stability is poor. Likewise, the lesions in the spinal cord, when advanced, as indicated both by the history and the neurologic examination of the patient, do not respond readily to treatment with liver extract, and may even progress under maximal doses of this substance. However, many patients with well defined evidence of combined sclerosis of the cord do show marked improvement, owing, in part or wholly, to systemic rehabilitation and restoration of muscular strength. As Fried [31] recently indicated, one may not reasonably expect great changes to occur when well defined neural lesions have developed, owing to the inability of nervous tissue to repair or regenerate.

SUMMARY AND CONCLUSIONS

One hundred and fifteen cases of pernicious anemia were studied with the following observations relative to neural symptoms and signs:

1. Ninety-five and six tenths per cent of the patients showed some evidence of neural involvement; 30.4 per cent had marked neural manifestations; 6 per cent had definite psychoses.

2. Improvement may occur in the neural and psychic changes in patients with pernicious anemia under treatment with adequate amounts

31. Fried, B. M.: Subacute Combined Degeneration of the Spinal Cord in Pernicious Anemia; Treatment with Liver Diet, J. A. M. A. **92**:1260 (April 13) 1929.

of liver extract, but may be due in part or wholly to improvement in the general condition.

3. In some cases arrest of the neural and psychic symptoms, without improvement or retrograde change, may occur.

4. Neural and psychic changes may develop for the first time or may steadily progress while the patient is being treated with daily amounts of liver extract adequate to maintain a normal erythrocyte level.

5. Liver extract apparently does not contain any specific antineurotoxic substance.

6. Regardless of the preceding conclusions, it is advisable to administer daily amounts of potent liver extract adequate to maintain the general health and normal level of red blood cells and to take precautionary measures in avoiding intercurrent infections.

7. During intercurrent infections or in the presence of increasingly severe neural manifestations, it may be advisable to administer maximal amounts of a potent fraction of liver.

Clinical Notes

EPILEPSY OF THE ANGIOSPASTIC VARIETY IN MONOZYGOTIC TWINS*

D. M. Olkon, M.D., Chicago

Human twins and twins of the animal kingdom generally have always been objects of interest because of their striking external similarity. Human twins of complete identity or, as they are technically designated, identical or duplicate twins, are of special interest because of their identical sex and external likenesses. The twins of this report are of double interest, (1) because of the apparent external identity of features and sex and (2) because of a like pathologic disturbance found in them, namely, that of "genuine epilepsy."

REPORT OF A CASE

The twins came to the clinic on Feb. 3, 1927, because of "epilepsy," and since then I have observed them from time to time. Glen and Irvin, later to be referred to as G and I., were identical twins, born one minute apart in 1916. The history of the parents and of their known relatives was without significance. Twinning, epilepsy, alcoholism and syphilis were denied in the families of the parents. The father was of German and the mother of Polish birth; they were apparently in good health. There were two older brothers of the twins, who were also well. The age of the mother was 29 when the twins were born. The history of this twin pregnancy is without clinical importance. The mother was in good health throughout the period of gestation. Labor was spontaneous, lasting about six hours. At birth, G. weighed 4½ pounds (2 Kg.) and I. weighed 4¼ pounds (1.9 Kg.). They were breast fed, and their growth and development continued in a normal way.

At the time of examination, G. was 57⅘ inches (146 cm.) tall and weighed 89 pounds (40.3 Kg.) while I. was 58⅘ inches (149 cm.) tall and weighed 89¼ pounds (40.4 Kg.). Teething, walking and talking began in the last months of the first year, and the patients walked steadily and talked at the age of 2 years. There is no history of enuresis after the second year. The subsequent school record for learning and behavior was good, and at the age of 12 years and 6 months they were finishing the seventh grade in the public schools.

G. and I. were of nearly the same height and weight; their blond hair and blue eyes could not be told apart, and the color and texture of their skins were identical. The height of the foreheads from the bridge of the nose to the hair-line measured the same within 2 mm.. The length and circumference of the arms, the shape and length of the fingers, thumbs and finger-nails and the lanulae measured nearly the same. The same type of irregularities were found in the teeth; the dental arches and occlusion, measured from plaster of Paris models, were identical. In a word they appeared to be true duplicates. Hence I

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* From the Divisions of Neurology and Psychiatry, University of Illinois, College of Medicine.

shall not record all of the measurements made in greater detail. Nature, indeed, had slavishly followed the same set of "blue prints" in this instance to the most insignificant detail, as is seen to some extent from the photographs (fig. 1).

History of Convulsive Attacks.—The history of the attacks throws some light on the type of the convulsive state. When 20 months of age, the boys were observed by their mother one day to be constipated; in order to relieve the constipation they were given raw apples to eat. That evening, G. had a convulsion which lasted for a few minutes, and about five minutes later I. had a similar convulsive attack of about the same duration. (The mother "blamed the apple.")

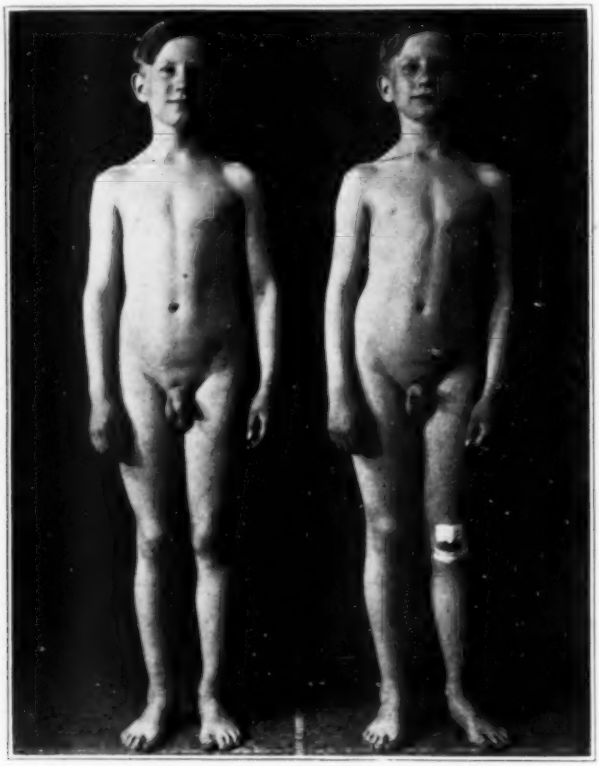

Fig. 1.—Photograph of the twins.

They made complete recoveries and were free from disturbances for two years. The seizures as described by the mother seem to have been typical epileptic attacks, with tonic and clonic spasm and loss of consciousness and without any noticeable after-effects.

Two years later, i. e., when they were 3 years and 8 months of age, they again had convulsions. I. had an attack in the morning and G. in the evening; these attacks were similar to the former ones. On this occasion also they were preceded by a day of constipation. Once more they were free from attacks for over two years.

When 6 years of age, the boys contracted measles, and during the period of fever again became constipated; this condition was again followed by convulsions,

one each day, for two successive days. They made a rapid recovery from the measles, but from that time on the convulsions continued to appear at more frequent intervals. The boys were now seen by a physician, who prescribed for the attacks; notwithstanding the medication, the convulsions continued to appear at frequent intervals.

Four years ago, during a visit to the clinic, both boys had typical "grand mal" attacks, which gave me an opportunity to observe the character of the convulsions, the postepileptic status and the aftermath of the capillary changes in the superficial vessels of the skin; these will be described later.

Examination.—Laboratory tests were made of the blood for the percentages of sugar, chlorides, urea and nonprotein nitrogen, creatinine, calcium, cell sedimentation, differential count, coagulation time and p_H estimation. All tests gave normal results, and the Wassermann and Kahn tests for syphilis were negative. The van den Bergh liver function test and kidney function test showed these organs to be normal. No abnormalities were found in the urine or feces. Roentgen examination of the head, sella turcica, sinuses, long bones and thymus region, as well as fluoroscopic examination of the chest disclosed no abnormalities or irregularities of any kind. The tonsils were removed, and the boys were also circumcised. The basal metabolic rates were plus 4 and plus 7, respectively.

Neurologic examination did not disclose any apparent gross abnormalities. All reflexes were present and equal on the two sides in both boys, and there were no abnormal reflexes. The eyegrounds, eye muscle tonus and vision were normal.

The Capillary System.—Observations of the superficial capillaries of the skin were made over the dorsal side of the hand above the third metacarpal joints between the little and ring fingers, above the thumb and between the index finger over the prominent part of the first and second metacarpals, above the third phalanx of the middle finger, above the radio-ulnar articulation of the wrist, over the skin in the region of the trapezius in the scapular area, over the skin in the region of the pectoralis major muscle in the mammillary line, over the skin of the abdomen to the side of the umbilicus and over the skin of the shaft of the first phalanx of the great toe.

Type of Microscope Used.—The observations were made by means of a Zeiss capillary microscope which was devised by Otfried Müller. (I use a compensating ocular 6 with it.) This microscope has a magnification of from 60 to 100 diameters; a 6 volt lamp is contained inside the tube of the microscope. The advantage of this instrument over others is that the light is direct and as the focus moves, the light moves with it so that the degree of illumination does not vary. Only a small amount of heat is given off by the lamp, so that no appreciable vasodilation from it is noticeable. Cedar oil or glycerine is spread over the fields of observation, which gives a clearer vision.

The illustrations in this paper are from observations and drawings of the third phalanx of the middle finger, the dorsal side in the region and over the metacarpal bones between the little and ring fingers, between the thumb and index finger, above the wrist and over the first phalanx of the great toe.

Figure 3, however, was not obtained from the twins. It is a photograph of the archicapillaries of the nail fold, showing great dilatation with roughened walls and the vessels partly empty of blood; it was published by Hans Delbrück.[1] A copy of this photograph was included because similar changes in the archicapil-

1. Delbrück, Hans: Archicapillaren und Schwachsinn, Arch. f. Psychiat. **81**:606 (July) 1927.

laries of the nail fold were observed in my patients. The nail folds, however, do not furnish as adequate information concerning the structure and behavior of the capillaries as the drawings of the parts of the body already enumerated.

Observations of the Structure and Behavior of the Capillaries of the Twins: The likeness and distribution over the areas of observation was unusually striking in the similarity of appearances. Never before have I seen two separate persons with nearly the same pattern, both during a quiescent period and following a convulsion. I have observed many "fraternal twins," normal and epileptic, but in them the capillary similarity was no more than the usual resemblance generally seen in nonrelated persons.

During the quiescent period in the twins, the "comma-like" capillaries were greatly thickened and closely grouped, with many irregularities. Some were empty, some elongated, of toy-balloon shape, some crescent-shaped and some in which the crescent seemed pinched in the center (fig. 2*A*). The larger capillaries were dilated, partly empty and atonic, and their walls were thickened (fig. 2*B*). Some

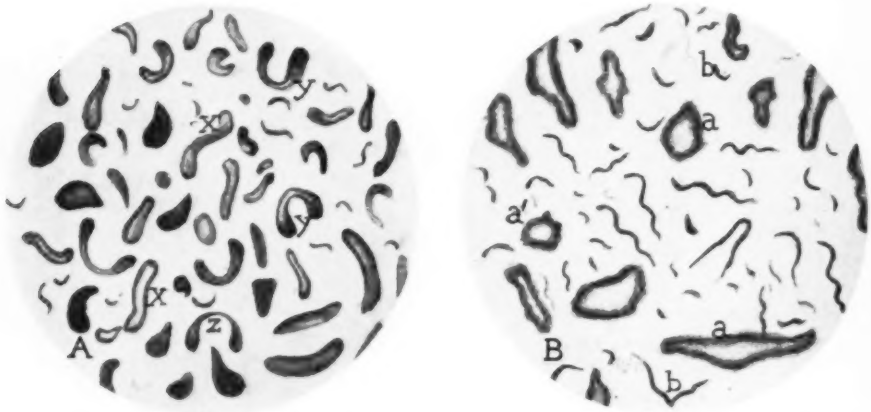

Fig. 2.—*A*, various distortions and disfigurements of the capillaries of the twins: *X*, elongated toy balloon shape; *Y*, crescent form; *Z*, the crescent shows constriction in the central portion. *B*, dilated, atonic and partly empty capillaries: *a*, ameba-like forms, partly empty, with pseudopod-like projections; *a'*, a capillary assuming an almost globular form with a markedly thickened wall, partly empty; *b*, tonic capillary stasis and marked tortuosities of the contracted capillaries.

of the large capillaries were so greatly dilated that they appeared not unlike distorted amebae. (A small capillary is one through which only a single file of blood cells can pass, and a large capillary allows more than one blood cell to pass through the lumen transversely.)

Irregularity and deformity of the vessels was also seen in the archicapillaries, as well as in the subpapillary plexuses (fig. 3).

Following a convulsion, hemorrhages in the superficial capillaries were abundant and in character not unlike those found in the pia-arachnoid, lungs, liver, skin, etc., of a dog after an experimental convulsion, as has been described by Olkon and Joannides.[2]

2. Olkon, D. M., and Joannides, M.: The Capillary Circulation in the Alveolus Pulmonalis of the Living Dog, Arch. Int. Med. **45**:201 (Feb.) 1930.

While the boys were under treatment, after six months' freedom from convulsions, observations were again made of the capillaries, but the patterns showed slight change. Some of the vessels, however, showed fewer deformities than had formerly been observed.

In order to ascertain the stability of the improvement, hyperventilation was used as a test, with the result that in both boys tonic and clonic convulsions developed which lasted for ninety seconds, with loss of consciousness for thirty seconds; following it there was a phase of respiration and heart action that resembled an Adams-Stokes syndrome, namely, bradycardia with a radial pulse rate of about 50 per minute, associated with a jugular venous pulse rate of about 80 per minute with periods of asystole and momentary attacks of syncope. The discrepancy that existed between the radial and jugular pulsations, the asystole and the syncopal attacks resembled the Adams-Stokes syndrome, for there were no indications of a specific disease of the conductive mechanism of the heart or of the myocardium; the interesting feature in this occurrence is that it shows the

Fig. 3.—Photograph of greatly dilated archicapillaries of the nail fold with roughened walls and some only half filled with blood (after Delbrück). Similar changes of the nail fold archicapillaries were also observed in the twins.

grave changes that a vasomotor spasm and its imbalance may produce. The boys, however, quickly recovered from this attack. During the attack and the unconscious state I glanced at G.'s capillaries. They looked massed together; some were dark, some pale and empty, and some were broken, with free blood elements near the point of rupture (fig. 4). Immediately after the convulsions, the changes resembled those already described, and there was also noticeable spasm in the large capillaries (fig. 5).

Treatment.—On the basis of the violent angiospasm,[3] a diagnosis of spasmophilic epilepsy was made, and antispasmodic treatment was instituted, with the result that the attacks became greatly reduced until the twins were practically free from seizures and remained so for over three years.

A ketogenic diet, which was adequately carried out, had no influence on the frequency of the convulsions in this instance.

3. Olkon, D. M.: A Case of Vascular Spasm Giving Rise to Epileptic Phenomena, Arch. Neurol. & Psychiat. **17**:857 (June) 1927.

Fig. 4.—*a*, ruptured capillaries with free blood cells near the points of rupture: *b*, a spasm of the capillary; *c*, constriction near the rupture and dilatation at the point of bifurcation forming an empty archicapillary; *d*, part of the capillary containing immobile blood cells.

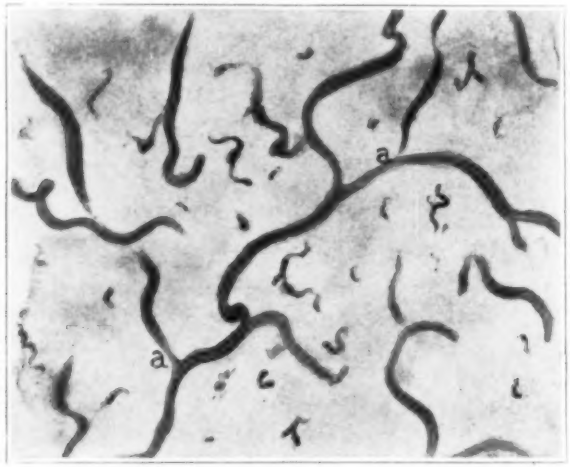

Fig. 5.—*a*, spasm with atony, and thickened walls of the subpapillary plexuses. Between the subpapillary plexuses many broken and congested smaller capillaries are seen.

COMMENT

Many interesting questions arise in this connection: (*a*) Was the effector in this particular instance introduced through the zygote? (*b*) Can early trauma produce identical disturbances in duplicate twins at the time of birth? (*c*) Is it known that genuine epilepsy has ever been transmitted by way of the zygote, when there is a possibility of its having been absent or recessive in the two families for at least three generations? Investigations on human twins have been recorded in the literature by many observers. It is only in recent years that intensive studies have been carried on with the discovery that there seems to be a certain ratio of appearance, to be mentioned later.

Geoffroy St. Hilaire,[4] in 1832, gave an extensive account of investigations of animal and human twins, and Spaeth,[5] in 1860, also reported extensive studies on human twins. Later, Ahlfeld,[6] in 1878, undertook more detailed investigations of human twins in their relation to abnormalities and monstrosities. Since then many careful investigators have shed further light on this problem. Wilder,[7] in 1904, studied duplicate twins and double monsters, and formulated certain hypotheses as to their production. The most comprehensive investigations concerning twins, however, up to the present time are those of Newman[8] and his co-workers. Arey,[9] in 1922, took up the study of identical twins with reference to the anatomic identity of organs. Newman,[10] in 1923, however, greatly enriched knowledge of the nature of twins both in animals and in human beings, clarified erroneous notions and established a biologic classification of twins.

Darwin[11] considered twins a "sport" which appears from time to time in nature, but Nichols[12] found a certain "frequency of occurrence;" he stated that identical male twins occur in 1:264,497 births, male and female twins in 1:264,098, and female twins in 1:219,312. These figures refer only to the frequency of monozygotic twins. In dizygotic twins, according to Newman, the sex predetermination has a different ratio, but this does not concern my discussion.

While embryologic, physiologic and sex variations have been intensively studied, "genuine epilepsy" in identical twins is still rare in the literature.

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TREATMENT

After phenobarbital, bromides and a ketogenic diet had been tried without noticeable reduction in the number of convulsions, the boys were given tincture of belladonna, 3 minims (0.18 cc.) four times a day; the dose was increased to 5 minims (0.31 cc.) four times a day with 10 grains (0.65 Gm.) of calcium lactate daily. This was given in divided doses, with the result that the convulsions became less frequent; when they did occur they were of shorter duration and milder type. The boys have now been free from attacks for over three years.

At the present time 5 drops of tincture of belladonna is still given twice daily as an empiric means of preventing the convulsive state, if possible, with the object of establishing thereby a "no convulsive habit."

SUMMARY

1. "Genuine epilepsy" was encountered in identical male twins.

2. The type of epilepsy seems to have been spasmophilic.

3. Antispasmodic medication in this instance was more beneficial than bromides, phenobarbital or a ketogenic diet.

310 South Michigan Avenue.

ACUTE DIFFUSE ENCEPHALITIS

A Report of Two Cases *

GEORGE B. HASSIN, M.D.

Professor of Neurology, College of Medicine, University of Illinois; Histologist to the State Psychopathic Institute

AND

SAMUEL J. HOFFMAN, M.D.

CHICAGO

Acute inflammatory conditions of the central nervous system do not, as a rule, give signs of a tumor of the brain, such as papilledema, for instance. Although they are mentioned in very few instances, such changes in the optic nerve are of great practical importance for, in suggesting the possibility of a tumor of the brain, they may lead to a wrong prognosis and improper line of treatment. As instances, two cases are here briefly recorded.

REPORT OF CASES

CASE 1.—*History.*—C., a boy, aged 11 years, admitted to the pediatric service (Dr. Julius Hess) of Cook County Hospital on Jan. 24, 1929, during the previous two weeks, had had frequent attacks of vomiting and headaches, pain in the upper portion of the abdomen, "soreness in both ankles" and a mild dry cough. The delivery was normal. The patient had never had convulsions or other ailments. One year previously, he spent about four days at the Cook County Hospital "after

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* From the Neurologic service of the Research and Educational Hospitals of the University of Illinois and the Pediatric Service of Cook County Hospital.

he had had some fruit." The parents said that he had not had constitutional or any other diseases.

Examination.—The patient was emaciated; his temperature was 100.8 F., the respiratory rate was 20, and the pulse rate, 64. The teeth were decayed; the tonsils were large, and the tongue was coated; the glands of the neck were enlarged. The pupils and the cranial nerves showed no changes; signs of paresis or paralysis of the extremities were absent, though the active movements were weak and the coordination was poor. The triceps, biceps and patellar reflexes were present; the achilles jerk was lively bilaterally with a transient clonus; the plantar reflex gave a normal flexor response, and the upper abdominal reflexes were absent. Sensibility was normal. The fundi showed bilateral papilledema. A spinal puncture, performed two days later, yielded a fluid under moderately increased pressure; it contained 10 cells per cubic millimeter and gave a negative reaction to the Pandy test.

Examination of the heart revealed bradycardia; there were no changes in the lungs or the abdominal organs; the bowels were regular, and the appetite was good.

In walking, there was a tendency to keep the head bent to the right and to fall to the right when the eyes were closed; a "past pointing test was positive."

On February 6, examination by Dr. Boot revealed past pointing to the right with the left hand, which was ataxic; a marked nystagmus response and past pointing on caloric stimulation of the right ear, while such stimulation of the left ear produced neither nystagmus nor past pointing; in addition, there was a marked choked disk. Dr. Boot felt justified in making a diagnosis of tumor of the left side of the cerebellum and of the left vestibular nerve. This diagnosis was seemingly supported by the other signs and symptoms that were found on previous examination—headaches, vomiting, bilateral papilledema, bradycardia and the peculiar ataxic gait.

Course.—The patient was restless and complained of headaches and much pain in the back (Jan. 27, 1929); he moaned a great deal, occasionally showed air hunger (gasped for air), often vomited, and some days was listless. During the next three weeks, the temperature was mostly normal; once it rose to 102 F.; but the headache and vomiting were severe.

On February 14, a hemiplegia of the right side developed, with involvement of the lower part of the right facial nerve, inability to protrude the tongue and drooling of saliva; the fundi exhibited a marked optic neuritis, especially on the right side, but the visual fields, on rough test, appeared normal; speech and deglutition were difficult; mucus came from the mouth, and the patient was practically helpless. By February 22, the condition became so alarming that a neurosurgeon recommended ventriculography for the purpose of determining the possible cause of the increased intracranial pressure.

When seen by one of us (G. B. H.) on March 12, the patient showed a complete hemiplegia of the right side with involvement, on the same side, of the motor fifth, ninth and tenth nerves, and paralysis and atrophy of the tongue and inability to talk, swallow or chew. In short, he presented the picture of bulbar paralysis with anarthria, which in the presence of signs of increased intracranial pressure and the previous signs recorded suggested a multiple lesion of the brain. As multiple, rapidly growing tumors (hypernephromas, for instance) may give such a picture and a rapid course, it was thought that a ventriculography or surgical procedures would be of no benefit.

At this time an examination of the eyes by Dr. St. Germain revealed only hyperemia with slight blurring of the borders of the disks; there was no disproportion in the size of the arteries and veins. The amelioration in the condition of the eyes was evidently a manifestation of the beginning of a general improvement, for on March 26 the patient began to move the right leg and arm and could swallow and chew, and on April 6 he was able to feed himself and drink from a cup. The tongue, however, was immobile. On March 26, the vision in both eyes was 20/15, the disks were "practically normal," and the patient was able to move somewhat the paralyzed extremities. One month later, examination revealed marked dysarthria with understanding of speech preserved, and slight weakness and tremor of the right arm and leg, especially on attempts to move them or to walk; the reflexes were exaggerated throughout, and a typical Babinski sign was present on the right; the uvula did not move on phonation, and the tongue did not move beyond the teeth. The pupils and fundi were normal.

While the diagnosis of multiple or disseminated lesions of the brain was plausible, the nature of the latter was thought to be inflammatory—a disseminated or diffuse encephalitis.

The laboratory observations were either negative or of little value. For instance, cultures from the nose and throat were bacteriologically negative; roentgenograms of the skull and chemical studies of the spinal fluid as to the content of sugar gave negative results. Once the temperature was as high as 103 F., with a pulse rate of 120 and a respiratory rate of 24; as a rule, however, the temperature was normal or only slightly elevated. The patient's condition grew steadily better, and on May 1 he was discharged.

Reexamination on May 5 revealed a typical hemiplegic gait with a wide circumduction of the right lower extremity; the right nasolabial fold was obliterated; the teeth were carious; the uvula, soft palate and pharynx were normal; the eyes showed no nystagmus, and their movements were normal; the pupils were equal and regular and reacted well to light and in accommodation; active movements of the upper extremities were performed freely; the right lower extremity was somewhat rigid, and the tendon reflexes were exaggerated, especially on the right, with a rather indefinite Babinski and a definite Rossolimo sign on this side. Genito-urinary disturbances were absent, and the disks were perfectly normal. The patient attends school willingly and regularly and produces an impression of a mentally normal, contented child.

Comment.—It is probable that had the changes in the eye been absent, a diagnosis of tumor of the brain would not even have been suggested. Neither the onset, which was rather acute, nor the occasional presence of an elevated temperature precluded the possibility of a tumor of the brain. It is known that cerebral tumors, especially in children, may run without or with only a few signs or symptoms, and cerebellar tumors may be accidental discoveries at necropsy. In this case the course was rather progressive. It showed first as a cerebellar lesion because of ataxia, dizziness and past pointing, then as a motor cerebral lesion (hemiplegia) and finally as bulbar paralysis. In short, the clinical picture indicated a disseminated lesion of the brain in the presence of signs of increased intracranial pressure and a practically normal temperature. The disseminated lesion, thought at first to be neoplastic, proved to be inflammatory, and was decidedly atypical in its course. It was atypical because disseminated lesions of the brain may vary ad infinitum, depending on the localization and the amount and extent of the structures involved. In this case the cerebellar symptoms predominated for some time, and it is remarkable that they were also in the foreground in case 2.

CASE 2.—*History.*—Frank B., aged 17, entered the Research Hospital of the University of Illinois on Jan. 15, 1930, because of headaches, inability to walk, double vision, occasional vomiting and loss of weight. He had been working in a battery shop, where he came in direct contact with lead; he was engaged in soldering plates together and placing them in cells. On Oct. 15, 1929, after working there for five and one-half months, he was seized wtih severe abdominal pain, dizziness and headaches. He had to give up work and felt better for a short time. On November 10, however, the headaches became much worse, diplopia developed and vomiting set in.

Examination.—The patient was emaciated and had marked photophobia and an inward squint of the left eye. He was able to stand when supported, and in walking showed a tendency to fall to the right and backward. The left hand exhibited incoordination, tremor and adiadokokinesia; muscle power, speech and mentality were normal. The tendon reflexes were much diminished and could be obtained only with reinforcement, while the radial and ulnar jerks and the skin reflexes (abdominal, cremasteric and plantar) were normal. Sensibility was apparently reduced; the stereognostic and position senses were normal. There were: anosmia on the left side; paralysis of the left abducens nerve, and bilateral papilledema, with preservation of the temporal quadrants, the elevation of the disks being 3 diopters in the left and 2 in the right eye. On rough examination, the visual fields were found to be normal (cooperation was rather poor). Other cranial nerves were normal.

Laboratory Examinations.—Examination of the blood showed: hemoglobin, 75 per cent; red cells, 4,900,000; white cells, 9,200, of which 21 per cent were lymphocytes, 74 per cent polymorphonuclears, 3 per cent mononuclears and 2 per cent eosinophils. No stippling of red cells was seen in spite of careful study. Chemical examination of the blood revealed: sugar, 87 mg. per hundred cubic centimeters; nonprotein nitrogen, 36, and a negative Kahn test.

Roentgen examination of the skull in a lateral direction showed no changes; the sella was practically normal. The temperature was normal; the pulse rate was 80, and the respiratory rate, 20.

Vestibular examination by Dr. Schneck showed the "medulla and the tracts to the cerebrum intact but an interference with the past pointing." The conclusion was a "probable cerebellar lesion."

Course.—After three months the patient's condition began to improve gradually. On February 5, the swelling of the disks was only 2 diopters and two weeks later it was 1.5 diopters, involving only the nasal two-thirds. On February 9, he was able to walk unaided and felt stronger. On February 28, the left knee reflex could be obtained with reinforcement, but the right knee reflex was absent. On March 6, both knee reflexes could be obtained without difficulty; slight diplopia was still present, especially after prolonged reading. On April 19, reexamination revealed: the movements of the eyes were practically normal; the disks were pale, especially in their temporal portions; the papilledema had disappeared entirely; the tendon reflexes were present throughout, and gait and speech were normal. The patient felt practically well and complained only of a slight weakness in the left leg.

The difficulties in the diagnosis in this case were considerable. The history of lead intoxication, as manifested by the abdominal pain and constipation, severe headaches and vomiting and the changes in the blood observed by the family physician, made a diagnosis of encephalitis due to lead probable. The rapid development of a bilateral choked disk, with absent patellar reflexes and marked cere-

bellar symptoms also suggested the possibility of an encephalitis or an encephalopathy due to lead. Such a condition may occur acutely, but, as has been shown elsewhere,[1] is incurable. In this case it was evidently of a different origin, probably an infection; that is, it was acute encephalitis.

When reexamined on May 19, the patient showed slight nystagmus on looking to the left, a pallor of the temporal halves of the disks, occasional diplopia, normal tendon and skin reflexes, no tremor and good muscle power throughout.

Comment.—The foregoing signs and symptoms resemble some features of multiple sclerosis which, according to some authorities, may result from an acute disseminated encephalomyelitis. However, a diagnosis of multiple sclerosis in this case would not be permissible because of the absence of abnormal tendon and the presence of normal abdominal reflexes, and mainly because of the rapid course. Acute multiple sclerosis would be a more proper diagnosis, but such a morbid condition is practically the same as disseminated encephalomyelitis.

COMMENT

The theoretical as well as the practical value of the two cases recorded is great. While both patients recovered, the recovery was not complete. One patient had a permanent hemiplegia, the other a partial optic atrophy. Whether other sequelae may be expected, such as are seen after epidemic encephalitis, is hard to tell at present.

One more feature should be mentioned. In former years, cases like those here recorded used to be diagnosed as pseudotumors. From careful histopathologic studies,[2] they proved to be inflammatory conditions, that is, cases of encephalitis, and are no longer diagnosed as pseudotumors. Though our cases differ from "pseudotumors" in the acute course, the pathologic conditions are probably alike and may show only quantitative differences. Histologic studies, however, so far are lacking.

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News and Comment

NAME OF NARCOTICS DIVISION, PUBLIC HEALTH SERVICE, CHANGED TO DIVISION OF MENTAL HYGIENE

In a recent report, Surgeon General H. S. Cumming of the Public Health Service indicates that the year ending June 30, 1930, has been characterized by additional legislation seeking to coordinate and crystallize the functions of the Narcotics Division, now designated by law as the Division of Mental Hygiene.

At the close of the year, the functions of the Division of Mental Hygiene, in the office of the Surgeon General, included the administration of the two recently authorized United States narcotic farms; studies and investigations of the nature of drug addiction and the best methods of treatment and rehabilitation of persons addicted to the use of habit-forming drugs; the dissemination of information on methods of treatment and research in this particular field; cooperation with state and local jurisdictions with a view to their providing facilities for the care and treatment of narcotic addicts; the supervising and furnishing of medical psychiatric service in federal penal and correctional institutions; studies and investigations of the abusive use of narcotic drugs and the quantities of such drugs necessary to supply the normal and emergency medicinal and scientific requirements of the United States; and studies and investigations of the causes, prevalence and means for the prevention and treatment of mental and nervous diseases.

The site for the first United States Narcotic Farm has been selected at Lexington, Ky., and plans are under way for the development of the necessary buildings thereon. Medical officers have been assigned to the medical and psychiatric clinics established at the several penal and correctional institutions.

BACK ISSUES OF MENTAL HYGIENE

The National Committeé for Mental Hygiene, announces that a limited number of back issues of *Mental Hygiene,* beginning with volume 1, 1917, are available, without charge, to libraries, medical schools, hospitals, clinics and other eleemosynary and educational institutions. The only charge will be for packing and shipping. As this offer will stand for but a few weeks, applications should be made at once to H. Edmund Bullis, Executive Officer, The National Committee for Mental Hygiene, 370 Seventh Avenue, New York. Orders should be sent for as complete sets as possible.

Abstracts from Current Literature

THE TARDY FORM OF AMAUROTIC IDIOCY (BIELSCHOWSKY TYPE). G. MARINESCO, J. f. Psychol. u. Neurol. **41**:1, 1930.

Marinesco describes clinicopathologically a case of the hyperkinetic form of amaurotic idiocy in a male child at the age of 5½ years. The disease began at the age of 4, and in addition to the usual clinical features of amaurotic family idiocy with simple optic atrophy, it was characterized by the presence of cerebellar symptoms with hyperkinesia.

Sections stained with the Nissl stain (Giemsa) showed chromatolysis going as far as achromatosis of the nerve cells; this was most marked in the cerebral cortex, although a few cells with fairly well preserved chromatophil substance could still be seen. In the cells of the cerebral cortex, and especially in those of the spinal cord, there was noted a more or less intact perinuclear zone indicating that the disease of the cells advances from the periphery toward the center and involves the cytoplasm, leaving the nucleus relatively intact. This, according to Marinesco, is of significance in view of the rôle played by the protoplasm of the cell in the transmission of hereditary and familial diseases.

With the Cajal and Bielschowsky stains, the neurofibrils of the body of the dendrites and of the lateral dendrites going toward the surface of the cortex were well preserved, whereas the endocellular network, as well as the neurofibrils of the dendrites which emanate from the base of the cell, showed profound alterations. In the pyramidal giant cells the superficial neurofibrils were reduced to a thin thread surrounding the contour of the cell. With all stains the nuclei of the various cells of the cortex were intact or almost so. The plexus of nerve fibers, especially of the first layer of the cortex and those forming the supraradiary and interradiary fibers, showed rarefaction.

It was noteworthy that there were no cells throughout the entire cerebral cortex that had preserved their integrity and that the intracellular network was profoundly damaged.

With the Weigert-Pal stain, there were seen a considerable number of cells whose cytoplasm contained a small quantity of intensely dark stained granules and others in which the granules appeared less dark and unevenly distributed throughout the nuclear part of the cell. There were also observed cells containing a few grayish, fine granules or a mass of granules that could scarcely be made out even with an oil immersion lens. Finally there were seen some cells containing compact masses of fine or coarser granules in which the outlines appeared indistinct and which occupied either a segment only or an entire cell body.

With the Heidenhain stain, the nerve cells appeared deep black because the lipoids within them take up the hematoxylin. In some areas the stratification of the central lobule was somewhat indistinct and there were also seen a number of microglia cells that took the stain as well as the nerve cells themselves. The putamen could be clearly distinguished from the adjacent pallidum. This, according to Marinesco, would seem to prove that the pallidal cells and the proliferated neuroglia contain more lipoid substance. As has been previously pointed out by Marinesco, in Tay-Sachs's disease glycogen is found not only in the neuroglia and microglia (?) cells but also in the nerve cells, whereas in the tardy form this substance is found neither in the neuroglia cells nor in the microglia elements. This difference is explained by the fact that in new born animals glycogen is found in all radicular nerve cells and in the large cells of the cranial nuclei, but it disappears as the animal becomes a few weeks older. It is very likely then that in the infantile form of the disease in question, the glycogen is not utilized but is deposited in the nerve cells, whereas in the more advanced stage the nerve cells utilize the dextrose.

A section of the cerebral cortex stained by the Graeff or Nadi method showed under a low power lens an almost complete absence of oxydase in the nerve cells. The same was true of the nerve cells in the subcortical centers and, in general, throughout the entire neuraxis, in the sympathetic nervous system and in the visceral vegetative ganglia, although the intensity of the reaction varied in different tissues.

Sections of the cerebral cortex and of the cerebellum stained by the Cajal method for neuroglia showed a definite increase in the number of neuroglia cells and a marked increase in their size; some of these had been transformed into astrocytes (fibrous neuroglia).

With the Hortega stain, there were observed characteristic microglial nests arranged in the form of rosets. The cells found in these nests were often unipolar with more or less considerable prolongations and ramifications. These cells are characteristic of amaurotic idiocy. Such microglial proliferation around the nerve cells is very common in this disease, and what is more important, the nerve cells themselves are occasionally broken down by the microglia cells and transformed into a granular body—a true neuronophagia.

In sections of the cerebellum stained with iron hematoxylin, the Purkinje cells appeared "overstained"; the molecular layer was reduced in size and the white lamellar layer remained intact. The Purkinje cells sending out the centrifugal fibers were only slightly affected. With the Bielschowsky stain, some of the Purkinje cells showed, ventral to the nucleus, a saccule extending into the dendrites; the cell body above the nucleus was greatly enlarged and filled with slightly stained lipoids. Other Purkinje cells contained two nuclei, and still others showed swelling of the axis cylinders. The neuroglia of the cerebellum (the Bergmann fibers) were swollen and increased in number; it was especially in the granular layer that there was an increased number of neuroglia cells with thick, long prolongations forming a network of inextricable entanglements in the parenchyma. A great number of ramifications were seen around the blood vessels and capillaries the walls of which showed no appreciable thickening.

From the histologic investigations of the cerebellum in this and in other cases, Marinesco is convinced that the fuchsinophil granulations are necessary for the new formation of dendritic ramifications.

Histologic examination of the viscera revealed the following: The anterior lobe of the hypophysis showed small masses or isolated lipoid granulations surrounding the nuclei of almost all granular cells. Occasionally an entire cell would be filled with this material. In addition to this lipoidosis of the hypophyseal cells there was also present a marked lipemia. A large quantity of lipoid material was found in the cortex of the suprarenal glands; it was more abundant in the fascicular region than in the medullary substance. The nerve cells in the latter contained a similar accumulation of lipoids in the cytoplasm. This observation is similar to that of the microscopic ganglia of the other viscera (intestines, liver and pancreas). In the spleen the cells of the malpighian corpuscles were considerably enlarged in size and were filled with lipoids in such large quantities that the nuclei were completely covered by them so as to render them invisible.

In the second part of the paper Marinesco discusses the relationship between Niemann-Pick's disease and the various other forms of amaurotic idiocy. He reviews the literature but adds nothing that is not already known.

In the third and final chapter he discusses the biochemical mechanisms of the different forms of amaurotic idiocy and their relation to autolysis. He points out that in amaurotic familial idiocy the nerve cells undergo characteristic degenerative changes. The cells filled with lipoid granulations become enormously enlarged and the dendrites, and occasionally also the axons, become swollen. This swelling of the cell body, dendrites and axons is, according to Schaffer, histologically an important feature in amaurotic familial idiocy. The swelling is a primary phenomenon, whereas the occurrence of products of degeneration, such as lecithinoids and prelipoids, is a secondary phenomenon. Marinesco regards

the lipochromia as an expression of autolysis preceded by the precipitation of the colloidal granulations which form a more stable compound with the lipoids. As far as the latter are concerned, it would seem that they have a double origin: (1) changes in the fuchsinophil granules; (2) a splitting up of the mitochondrias. Some observers (G. Biondi) believe that the fuchsinophil granules are identical with the mitochondrias, whereas others (Cowdry) regard them as two different kinds of formation. According to Marinesco, the fuchsinophil granules are pre-existing ultramicroscopic formations. During fetal life fuchsinophil granules are found in the nerve cells of the neuraxis and of the sympathetic and spinal ganglia; with advancing development of the cells, some of the fuchsinophil granules at the surface of the cell take up the reactions of the Nissl bodies by changing their character with changes in the acid-base equilibrum, following which the Nissl bodies stain blue and the fuchsinophil granules stain red. It is thus conceivable that the fuchsinophil granules and mitochondrias are formations resembling each other except as to their respective electrical charges.

Aside from the accumulation of lipoids in the cells of the neuraxis in the various forms of amaurotic idiocy, there also occurs a peripheral chromatolysis in most of the cells which is due to a disturbance of the protein metabolism. Thus Soula believes that the functioning of the nerve centers is always associated with a burning up of albumin. From this point of view there is a great difference between the functioning of a muscle, which utilizes carbohydrates and lipoids, and the functioning of the nerve centers, which consume the albumin from their own structure. But this consumption of albumin occurs not only under circumstances which enhance nervous activity (general hyperthermia, asphyxia, and convulsion-producing poisons which produce chromatolysis), but also following resection of a nerve which is accompanied by a central chromatolysis. Marinesco, in his researches on chromatolysis in nerve cells of experimental animals following injury to the peripheral nerves of these cells, found not only that the chromatolysis increased during the first days following the injury but that there was also a decided increase in the proteolysis of the cells. Chemical examination of these cells also showed that the proteolysis goes as far as the actual formation of amino-acids. The various phases which the proteins and lipoids undergo in this process of decomposition down to the formation of amino-acids are the same as those going on during the digestion of these substances in the digestive tract.

Another important fact to be remembered in this connection is that, as proteolysis increases, there occurs a liberation of ions, of which those of iron are the most significant because they play an essential rôle as catalyzers of oxidation. It would seem, then, that there occur in the various forms of idiocy metabolic changes in the cells involving all chemical compounds, proteins, lipoids, carbohydrates and ions (iron). Owing to these chemical changes there occurs an alteration of the cells in volume with resulting changes in their heat and kinetic energy and also in their surface tension, viscosity and tissue permeability.

To Marinesco the essential features of the pathologic process of the disease are: a diminution or disappearance of the oxydases, a change in the mitochondrias and neurosomes, a progressive diminution of catalyzing iron, the presence of glycogen in the cortical nerve cells (infantile form), an increase in the osmotic tension and a change of the intracellular p_H, running parallel with the phenomenon of autolysis.

The original article is in French and contains nineteen illustrations.

KESCHNER, New York.

THE RELATION OF HYSTERICAL CONTRACTURES TO CONJUGATE DEVIATION OF THE HEAD AND EYES WITH GENERALIZED RIGIDITY. G. MARINESCO and M. NICOLESCO, Rev. d'oto-neuro-opht. **8**:435 (June) 1930.

The resemblance between certain phenomena of epidemic encephalitis and those occurring in hysteria (vascular, thermic and secretory) has been the incentive for a careful study of the case here reported. The mental state of some patients with

encephalitis offers a certain degree of suggestibility which approaches hysteria, owing to an enfeebling of the function of inhibition. The phenomena of hysteria are easily reversible by persuasion, which is not possible with troubles due to organic lesion, but the present state of knowledge does not warrant the assumption that hysterical phenomena are not subject to the general laws that govern the functioning of the nervous system. All psychic or physiologic phenomena are the expression of a dynamic modification in the nervous system.

A woman, aged 36, complained of paroxysmal attacks of conjugate deviation of the head and eyes, occurring spontaneously and accompanied at times with rigidity of the limbs. There was nothing suggestive in the family or the past history. At the age of 20, after one year of marriage, she was separated from her husband on account of his drinking. There were no pregnancies. Suddenly, in January, 1920, she became maniacal, with cries, gesticulations, rebellious headache, absolute insomnia and crises of noisy tachypnea. This lasted three years, and she recovered calm and sleep after a visit to church. She then slept too much. In 1925, following an emotional shock, the first attack of conjugate deviation of the eyes appeared while she and a sister were alone. The attacks continued, sometimes every three or four days, at other times, several times daily. From the beginning, suggestion influenced the attacks. The attacks began by fixity of the eyes; the eyes then turned upward and to the right, and the head followed the movement of the eyes. The muscles of the neck were contracted, and no voluntary movement of the head or eyes was possible. At first, walking was possible during the attack. The crises lasted several minutes or even hours and disappeared spontaneously. Little by little, the attacks became generalized, rigidity of the limbs appeared and the patient could not walk or talk, although she could hear and comprehend everything. No new symptoms have arisen during the past six years. Anxiety, fear and groaning accompanied the attacks.

An attack could be brought on by fixation on a point, sometimes easily, sometimes with difficulty. After an injection of hyoscine this could not be done. Fatigue would induce a crisis; natural sleep caused the attack to disappear. The attacks became more severe and more frequent, requiring two injections of hyoscine daily, and without the hyoscine they sometimes lasted forty-eight hours. During the attack, the legs, the trunk and the head were in complete extension, the head turned to the right, the arms in hemiflexion, and there was considerable rigidity. If the patient were raised up, she stood on the toes, was rigid as a bar, and fell like a mass if not supported. Between the attacks her attitude resembled a slight parkinsonism. She was bent; the face was without expression, and she had a mechanical smile. Passive movements did not indicate an appreciable hypertonia, and the reflexes of posture were not exaggerated. The speech was rapid and monotonous; the gait was good, and movements of the limbs were rapid. The vegetative system was hyperexcitable; the test with intravenous injections of epinephrine showed a sympatheticotonia; the oculocardiac and solar reflexes were intense. During an attack, the vestibular apparatus became hypo-excitable, but it was normal between attacks. A simple chronic ulcer on the skin, which had existed for three years, was healed by the application of insulin to the wound. Hyoscine controlled the attacks but phenobarbital did not. The attacks could be stopped by ether anesthesia during the narcosis but they recurred with waking. Injections of distilled water had no effect. Suggestion, light massage and passive movements modified the rigidity temporarily. An Esmarch bandage relieved the rigidity below the point of application when on the arm, but it had no effect on the general rigidity or on the deviation of the eyes.

It would seem from the biologic and physiologic researches that all psychic phenomena are reduced to processes of excitation or inhibition which, in their turn, are effectuated by the aid of the nervous vibrations that depend on the migration of ions. This would indicate that there is no insurmountable barrier between the phenomena of hysteria and those of parkinsonism, with the difference that the former are reversible by suggestion, while the latter are not, and in order that the hysterical phenomena can occur, a special ground must preexist,

which is governed by humoral modifications and disturbances of vegetative innervation. The important fact with this patient is that it was possible at first to cause the disappearance of the contractures by suggestion. This case is, so to speak, a bond between an organic disturbance, such as a light parkinsonism following encephalitis, and a dynamic disturbance, such as hysteria. The frequent association of hysterical phenomena with epidemic encephalitis, the errors of diagnosis in postencephalitic parkinsonism, catatonia and hysterical contractures are facts that cannot be denied. All neuroses have a biochemical substratum, and hysteria is no exception. Numerous references to the recent literature are cited.

"In place of an accidental lesion suppressing the cortical interventions, as in pseudobulbars, a transient eclipse of the inhibitor control can be produced under the influence of a dominating idea, depriving all the reflex centers of their habitual moderating influence. This explains the similarity of these neuropathic accidents through all ages and in all countries."

DENNIS, Colorado Springs, Colo.

THE ETIOLOGY OF GINGER PARALYSIS. EDITORIAL, J. A. M. A. **95**:1672 (Nov. 29) 1930.

Within the past year a peculiar form of paralysis has afflicted many persons, particularly throughout some of the Midwestern or Southwestern states. Government experts have asserted confidently that the numbers of the patients run into the thousands, thus exhibiting what may reasonably be termed epidemic proportions. Evidence has rapidly accumulated indicating that the unique malady is closely associated with the drinking of fluidextract of ginger. The latter has been sold extensively for many years, since the introduction of the Volstead Act, for beverage purposes, because of a ruling of the Prohibition Bureau to the effect that the official fluidextract of ginger is a nonpotable beverage, thus removing the restriction from its sale. The disease that has come to be designated as "ginger paralysis" could scarcely have been caused by the familiar U. S. P. fluidextract; otherwise the morbidity would have been much greater and the incidence of the paralysis far more widespread. Many of the victims freely admitted having used fluidextract of ginger for years without effects other than those attributable to its alcohol content; hence the conclusion that an adulterated and poisoned product was being circulated for sale last winter.

An investigation was undertaken by the United States Public Health Service (*Pub. Health Rep.* **45**:1703, 1930; ibid. **45**:2509, 1930) as soon as the seriousness of the situation became manifest. Many puzzling features attended the early clinical examinations. The quantity of the ginger fluid consumed was apparently not the determining factor in the seriousness of the symptoms. A single drink is known to have produced essentially the same result as that following prolonged use of the product over a period of some days. Transitory alcoholic intoxication often occurred, as might be expected; but the really untoward symptoms were delayed, usually about ten days. The victims presented bilateral wrist drop and foot drop of varying degrees of severity. The picture became that of a flaccid paralysis for the most part of the distal muscles of the lower and upper extremities, pointing to involvement of the lower motor neurons localized in the lower lumbar and lower cervical regions of the cord. The unsuspected presence of arsenic or lead and other heavy metals in the beverage was soon ruled out by careful chemical examination of samples of the offending product. Phenol compounds were found to be present.

The familiar phenols, such as carbolic acid, are prompt in their toxic action, in contrast to the delay in the paralysis produced in the ginger victims. Confusion was added by the observation that, whereas rabbits and calves responded to the dangerous fluidextracts somewhat as the human victims did, monkeys seemed to be immune. The effective investigations of Smith, Elvove and their co-workers in the Public Health Service seem to have fixed responsibility for the unusual human disease on tricresyl phosphate, and more specifically on the triorthocresyl isomer. The pharmacology of this unsuspected product was not

known until the present occasion for its investigation. The systemic action of ordinary cresols is prompt; that of the cresyl phosphate is slow. It is assumed by the government pharmacologists to be absorbed as such, rather than hydrolyzed in the alimentary tract of man. It is further postulated that the substance has a special selective affinity for nerve tissue, where it may be disintegrated in situ. Such behavior would explain the long latent period in the onset of the paralysis and the persistence of the toxic action.

The details of the mode of action need to be worked out further, but the complicity of the triorthocresyl phosphate can no longer be doubted. Investigation and inquiry have revealed, by way of confirmation, that an adulterated ginger prepared by addition of technical tricresyl phosphate to U. S. P. fluidextract of ginger made to approximate the composition of the suspected toxic gingers behaved like them in phamacologic tests on susceptible animals. The precise reason for including triorthocresyl phosphate, which is now revealed as a highly specific poison, in commercial ginger extracts is not known. Smith and his colleagues regard it as reasonable to suppose that it was included there by unscrupulous producers on account of its physical or other properties that make it difficult to distinguish from the normal ginger constituents. Only a chemist of some ability, the government report adds, could have thought of this; and had there been anything known about the pharmacologic action of the substance and the possible dire consequences, it is probable that it would never have been used and the disasters would never have happened. The elucidating research illustrates what may be expected from the newly organized National Institute of Health, where the investigation of ginger paralysis has been prosecuted. Smith and Elvove have expressed a wonder whether there are not many other organic compounds of great pharmacologic interest, perhaps some with therapeutic possibilities, awaiting the attention of the pharmacologist. This question may well form the basis for part of the program of the National Institute. To unscrupulous manufacturers the study of the unexpected menace attending unwarranted adulteration of foods and drugs should be a lesson of far greater impressiveness than the mere fear of convictions and fines. The producers of the noxious ginger extracts have unwittingly become potential murderers rather than merely criminal purveyors of adulterated products.

EDITOR'S ABSTRACT.

PSYCHOPATHOLOGY OF SWALLOWING FOREIGN BODIES. W. KALDEWEY, J. f. Psychol. u. Neurol. **41**:309, 1930.

Kaldewey reports in the first part of this paper five cases of the swallowing of foreign bodies. This unusual condition occurred in more or less mentally deficient, asocial, hyperaffective and impulsive psychopathic patients with severe emotional changes which appeared suddenly and with primitive reactions. Some of them were constitutionally, and all of them psychically infantile. The striking feature in all of them was the repeated massive swallowing of indigestible, dangerous objects during periods of excitement and of more or less clouded consciousness due to hyperaffectivity. Occasionally these persons would also swallow objects when they were less excited and when the motivation for the act was not apparent. In many instances no relationship could be established between the act and some definite occurrence or experience in the nature of the fulfilment of a wish. Some of the patients were unusually anxious to undergo an operation. The author is unable to say whether the desire to be operated on is to be regarded as a "pleasure tendency" in the true sense of pleasure, or whether it is to be regarded as a desire to improve some "internal or external situation." He does not believe that the idea of a "pain sacrifice," as described by Trömner, is applicable to the patients whose cases are cited in this communication. Leppmann's explanation, however, that the boastful persons in this group do not possess sufficient intelligence to avail themselves of the finer hysterical mechanisms to achieve their strivings, seems reasonable to Kaldewey. Whatever else may be the reason for this peculiar psychic phenomenon, it is evident that these persons

feel that they have at least "accomplished" one thing, and that is that the world at large must be busy with them; they are very proud of the fact that they are "remarkable" persons, who gain great "notoriety" because the newspapers publish lengthy accounts of their "remarkable deeds."

The next question is why these people attempt to injure themselves by swallowing objects rather than by employing other methods. Kaldewey believes that the reason for this is their psychic infantilism. It is well known that even healthy infants and children put everything conceivable into their mouths; they eat coal, and lick up their urine and even their feces (psychoanalytically a "valuable product" coming from their own bodies). In this sense the swallowing of foreign bodies may be regarded as an infantile mechanism with the object of obtaining pleasure and wish fulfilment; these represent massive infantile and primitive archaic tendencies. Even to this day there are known to exist primitive people who devour disgusting substances and other objects for religious and mystic purposes.

It is remarkable how well the intestinal tract receives, harbors and finally eliminates these foreign bodies. Only in the rarest cases is an operative procedure necessary for their removal. In most cases large doses of castor oil and the eating of mashed potatoes are sufficient to cause the evacuation of broken spoon handles and open pen knives without the slightest untoward effect. Kaldewey, however, finds that these methods of elimination are extremely unsatisfactory to most of the patients; at the first opportunity they again swallow the same or similar objects and demand an operation. Another interesting peculiarity is the utter insusceptibility of these persons to pain. Whether this is due to a hypofunction or dysfunction of the perceptive sensory mechanisms in the brain or at the periphery, or whether there is a lack of sensibility from endocrine anomalies is difficult to say. In this respect there seems to be some analogy with the lack of sensibility occasionally observed in cases of dementia paralytica (Morzick).

The paper is concluded with the report of a case which differs from the other five because it deals with a feministic, impulsive and asocial psychopathic patient with a superabundance of fantasy; he worked very little and had all the earmarks of a vagabond and vagrant, although he was harmless and devoid of any tendency to criminality. He occupied his time by attending lectures on religion and lived the greatest part of his adult life in a monastery in which he performed odd jobs. This affected him so that he subjected himself to various pains and inflicted punishment on himself by swallowing masses of needles. It was his method of making himself, in martyr-like fashion, holy and divine by "killing his body." In this case, the author believes that the swallowing of the needles was a conscious and deliberate act under the influence of a religious fantastic goal. Later, swallowing the needles became associated with sexual pleasure. It is difficult to say whether or not this man was genuinely homosexual. Kaldewey is more inclined to believe that owing to his constitutional make-up he was unusually suggestible and at the same time lived his sexual life predominatingly in fantasy.

KESCHNER, New York.

ACUTE NEUROPTICOMYELITIS PRECEDED BY MILD MEDULLARY DISTURBANCES. H. ROGER, OPIN and J. SÉDAN, Rev. d'oto-neuro-opht. **8**:12 (Jan.) 1930.

A man, aged 47, was first seen on March 12, 1929. He had suffered for three weeks with fever and great general depression. For ten days before the attack, he had noticed tingling in the legs which was followed by hypesthesia. There had also been a feeling of stiffness in the arms. Vision began failing on March 10, and in two days was almost completely abolished. The eyegrounds on the right were normal, and on the left the arteries were a little contracted. Nothing abnormal was found in the nasal accessory sinuses. The Wassermann reaction of the spinal fluid was negative; the fluid contained albumin, 0.3 Gm., and 4 cells per cubic millimeter.

Neurologic examination on March 23 gave negative results, but on March 28 the reflexes were exaggerated, the muscular force was diminished, and there was slight difficulty in coordination. Treatment with bismuth was instituted, but was no more efficacious than a previous course of mercurial injections had been.

In June, an examination revealed: total discoloration of both disks; contraction of the arteries, contours sharp, retinas normal; moderate mydriasis; feeble reaction of the pupils to light; no motor deficiency; ocular tension normal; corneal sensibility normal. Neurologically, there was a diffuse syndrome of pyramidal excitation with exaggerated reflexes, which was most marked in the lower extremities; a Babinski sign was absent; an Oppenheim sign was distinct in the right foot; there was no dyssymmetry in the heel-to-knee test; there was slight motor deficiency; sensibility was equal on the two sides, and Lasègue's sign was absent. In the upper extremities, the reflexes were lively; there were slight adiadokokinesis and dysmetria on the left. The superior abdominal reflexes were lost, but the inferior were present. No paralyses of the cranial nerves were present. The vestibular tests gave negative results. The paretic disturbances preceded the ocular manifestations.

As to the origin of the disease, disseminated sclerosis was ruled out. Syphilis was eliminated through the past history, the laboratory examinations, the clinical evolution and the therapeutic test. Probably some neuraxic virus was blamable.

An interesting point in the case was the appearance of medullary symptoms before the optic disease, since in the majority of cases of ophthalmoneuromyelitis collected by Lapersonne in the last twenty-five years, the myelitis followed the optic neuritis. The suggestion is made that, in many cases, the myelitis may have actually been present, but was overlooked on account of its ill defined character. Only one similar case was found in the literature.

A critical review of the literature since 1889 is incorporated. In 1927, a histopathologic study of a case was made by Bouchut and Dechaume. The main points were: areas of disseminated myelitis of necrotic appearance, giving the aspect of cavities; discrete areas of degeneration of the pyramidal bundle, and perivascular leukocytic muff. The lesions were more marked in the gray nuclei, the peduncles and the anterior quadrigeminal bodies than in the pons and bulb. The optic nerves showed inflammation at the level of the meningeal envelope or the interfascicular partitions and around the vessels. There were patches in which the myelin had disappeared, and in which there were proliferation of the large multinuclear neuroglia cells and a moniliform appearance of the naked axis cylinders. "This syndrome, produced by a neurotropic virus, may give as a sequel a picture of multiple sclerosis and is probably only an anatomicoclinical modality of epidemic encephalitis."

DENNIS, Colorado Springs, Colo.

METABOLISM IN THE NERVOUS SYSTEM. EDITORIAL, J. A. M. A. **96**:116 (Jan. 10) 1931.

Until recently, textbooks of physiology have had little to say regarding the metabolism of the nervous system. One cannot penetrate far into the domain of muscle function before being brought face to face with problems of energy exchange. Consideration of muscular contraction inevitably is concerned with the production of work and heat; and such a process in turn involves the production of carbon dioxide and the utilization of oxygen. Nervous excitement and mental activitity also may increase metabolism; but, as Mitchell (General Physiology, New York, McGraw-Hill Book Company, 1923) has pointed out, no measurements of this increase have effectively eliminated the muscular contractions that accompany nervous activity. It is certain that most of the increase in metabolism, if any, that occurs during mental work is caused by contractions of skeletal muscles. They are active in maintaining a somewhat rigid posture of the body and in other ways, under these conditions. When complete muscular relaxation is maintained, Mitchell adds, all attempts to detect a rise in metabolism during mental work fail to yield decisive results. The brain constitutes only a

small portion of the body weight, so that a small rise in its rate of oxidative metabolism would have little effect on the sum total of the entire body. Emotional states may cause a marked rise in body metabolism; but this may be due to concurrent muscular contractions or to a secretion of calorigenic hormones.

There was a time when the nerves, in particular, were looked on as utterly inert carriers of nervous impulses, presenting an analogy to the conduction of electric currents along a metallic wire. The heat evolved by a nerve proved to be so extremely minute in amount that it became somewhat doubtful whether there is any metabolism in a nerve fiber. With respect to the masses of nerve cells such as are found in the brain, evidences of chemical changes incident to its function were not quite so negative as in the case of the nerve trunks. With the advent of delicate methods of investigation, the nervous system can no longer be regarded as an inert structure. Fenn (The Harvey Lectures, Baltimore, Williams and Wilkins Company, 1929) of the University of Rochester pointed out in his Harvey Lecture of 1928 that undoubtedly the most important fact that has emerged from all the investigations carried out on nerves is that the still somewhat mysterious wave of excitation differs fundamentally from most other waves, such as the pulse wave, sound waves and water waves, in that the energy to which it owes its progress is derived not from the mechanism or process that initiated the wave at its source but rather from the medium over which it is to pass. It is a sort of self-propagated wave of excitation.

The upshot of the latest observations is that in nervous transmission, unlike muscular contraction, oxidation is a necessary accompaniment (Fenn). Carbon dioxide is produced, as is a small amount of heat. The recent investigations of Holmes (Oxidation in Central and Peripheral Nervous Tissue, *Biochem. J.* **24**:914, 1930) at the University of Cambridge in England indicate that the various types of tissue composing the central nervous system have different rates of oxygen consumption. The activity of the gray matter is in this respect far greater than that of white matter. Evidently there are quite different types of metabolism in the brain and in the purely conducting parts of the nervous system. The rate of oxygen consumption of the conducting elements is of the same order, whether they are central or peripheral. In gray matter the metabolism is of a more intensive kind, different oxidizable substrates being involved. There can no longer be doubt that, in what Foster called the master tissues of the body, the brain as a whole uses oxygen at a much greater rate than does peripheral nerve.

EDITOR'S ABSTRACT.

THE EXISTENCE OF EFFERENT FIBERS IN THE POSTERIOR ROOTS OF MAN. O. GAGEL, Ztschr. f. d. ges. Neurol. u. Psychiat. **126**:405 (July) 1930.

There are two definite and different effects of electric stimulation of the peripheral segment of a transected posterior root: 1. Following the experimental demonstration by Stricker and Bayliss that faradic stimulation of the distal end of a transected posterior lumbosacral root in dogs and cats causes a definite vasodilatation in the hind foot, Foerster showed that such vasodilator effects are present also in man. His studies in man went even further than those in the animal, because he demonstrated these effects in the posterior roots of the cervical, thoracic, lumbar and sacral roots. Foerster showed that skin erythema in man has a definite metameral distribution, and that it is therefore an important method for the demarcation of dermatomes in man. Bayliss and Langley explained this vasodilator phenomenon by an antidromal conduction in the sensory nerve fibers. 2. The second effect of stimulation of the distal end of a transected posterior root is the inhibition of the secretion of sweat. This has been shown clearly by Foerster. It is well known that stimulation of an anterior thoracic root leads to the secretion of sweat in a number of dermatomes. If now the corresponding anterior and posterior thoracic roots are simultaneously stimulated, there is no secretion of sweat. A further effect of a pilo-erection occurs on stimulation of an anterior thoracic or upper lumbar root.

Ken Kuré showed in anatomic studies in dogs that after transection of a posterior root there are numerous fibers of thin caliber in the proximal segment that do not show degeneration.

Gagel investigated eight cases in man in which the posterior roots had been cut by Foerster for various reasons. The presence of efferent fibers in the posterior roots was investigated in these cases. He studied the central or proximal segments of the transected roots in serial section by the myelin sheath method. In all cases he found thin fibers in the proximal segment which were well preserved among the more numerous degenerated fibers. In his first case, one of multiple sclerosis, the time between operation and death was five years and three months. The fibers were of smaller caliber than normal, but were well preserved, and the difference may have been due to the disease process. Similar well preserved fibers were found in a case of tabes with transected roots, in which the patient died four years and nine months after the operation. Another case in which the patient died two years and twenty days after the operation showed similar intact fibers among the degenerated ones.

Gagel therefore believes that there are efferent fibers in the posterior roots of man, and that these fibers have their cells of origin in the spinal cord and not in the spinal ganglia.

From what cells in the cord do these fibers arise? Ken Kuré traced the cells of origin in dogs to small ganglion cells lying between the anterior horn and the substantia gelatinosa of the posterior horn. They showed retrograde changes. Gagel was able to investigate a case in which two posterior thoracic roots had been cut and in which the patient died twenty-nine days after the operation. Serial cell studies of the two segments of the cord concerned showed a decrease in the number of the middle-sized ganglion cells in the intermediary zone, but no retrograde changes were observed. He considered this observation inconclusive, and is studying the condition in apes.

ALPERS, Philadelphia.

STATIC CRISES IN A PATIENT A LONG TIME AFTER RECEIVING A CONTUSED WOUND OF THE EYE. PAUL REBIERRE, Rev. d'oto-neuro-opht. **8**:105 (Feb.) 1930.

A man, aged 38, was struck on the left eye by a gun barrel in 1916. The shock of the blow was severe, and a contused wound in the upper eyelid resulted. In the following days he suffered with headache and giddiness and with crises, which began with a sensation of tightness in the precordial region, extending to the base of the neck, followed by waves of heat in the face, and ended with the patient falling to the ground. Injury to the head did not occur in these falls. The crises would last a few minutes; return to a normal state was rapid and was not followed by a sense of fatigue. The general health was excellent, pneumonia having been the only previous illness. An attack occurred during the consultation. The patient slid out of the chair and collapsed on the floor, like a puppet when the strings are loosened; respiration was rapid but not stertorous; there were no clonus, trismus or hypertonus of the limbs; the pulse was not modified, and no foaming at the mouth occurred. There was complete corneal insensibility, and the patient seemed unconscious. After two minutes the corneal sensibility returned and, on request, the patient got up and was entirely himself again. He had no recollection of what had occurred during the crisis. Examination revealed a person of quite mediocre intellectual development with no neurologic abnormalities; the Wassermann reaction of the blood was negative, and the urine was normal. It is noteworthy that at the time of the injury there had been no loss of consciousness, ocular signs or symptoms of fracture.

These crises, as in certain old cases of concussion, are often neither frankly epileptic nor truly hysterical. They resemble the cases of sudden loss of postural control described by Ramsey Hunt as "static attacks." They are due to a reflex, starting in the scar of the peripheral wound and ending, via the sympathetic, in certain intracranial vasomotor nerves that have been sensitized by the primitive

shock, and are caused by an intracranial angiospasm. Typical epileptic attacks can be produced by spasm of the cortical vessels. Cases were observed during the World War in which pressure on even slight wounds of the face produced epileptic seizures. The phenomenon of repercussivity, described by André-Thomas, is explained by the observations of Barré: a distant irritation is echoed via the sympathetic nerve in an organ previously diseased, an old meningitis, for example. According to the nature and extent of this morbid territory, the crises vary and may even cross the boundary between the vegetative and the cerebrospinal systems, thus giving a fusion of symptoms and making classification difficult. Hysterical and epileptic crises are syndromes of diverse morbid phenomena. As in the case reported, a patient who requires a psychologic influence—the presence of the physician—in order to have an attack, who falls with prudence, has no convulsions and recovers in a perfectly lucid state is not an evident epileptic. On the other hand, one who loses consciousness, loses his corneal reflexes and has no memory of the attack and no disturbance of pulse or respiration has not a classic hysterical condition nor is he a malingerer. Therefore, as the terms hysteria, psycho-epilepsy and cataplexy are not fitting, the name "static crises" has been adopted.

DENNIS, Colorado Springs, Colo.

OCULAR NEUROSES. G. S. DERBY, J. A. M. A. **95**:913 (Sept. 27) 1930.

George S. Derby, Boston, believes that ophthalmologists produce more neuroses than they cure. The use of the eyes should be, and usually is, a subconscious function. Too often the neurotic patient is dismissed or got rid of with a minor change in his prescription, when what he really needs is a careful analysis of his condition and an explanation of how his various ocular aches and pains should be interpreted and treated. Far too many glasses are changed. Any one can find a slight difference in the strength of the lens or of the axis in any patient, however well the refraction has been done, and it is a fact that most persons can wear quite a number of different combinations of lenses with equal comfort, always provided the difference is not too great. Derby would banish the term eyestrain. If the general public could learn that eyes are seldom strained, this would be a much happier world to live in. The fact is that the eye is provided with a large factor of safety, and that healthy eyes do not become diseased even by excessive use. Frequently the system rebels and the trouble may center in the eyes. To do hard eye work one must keep the body fit. In at least 95 per cent of the cases a trained psychologist is not needed for either the diagnosis or the treatment. Rarely is it necessary to call one in. What is needed is a knowledge of human nature, sympathy, a willingness to spend some time in studying the case, and sound common sense. Fear is the commonest factor at the bottom of the difficulty; often there is some one blind or with very poor eyes in the family; this condition is impressed on the patient's mind and he fears that his own eyes are becoming affected. Frequently the fear is of that awful bugbear eyestrain, caused by some ocular pain or discomfort; or they fear that they are injuring their eyes permanently, that they cannot continue in their occupations, and perhaps cannot earn their living. Eyestrain is a terrible and serious bugbear to the public. Most of these neuroses occur in sensitive and highly organized people. Many cases can be recognized from the history alone. In many patients the diagnosis almost makes itself from the history of distress in using the eyes often relieved by a change of glasses, a long period of ocular disorder, many pairs of glasses, a person of the sensitive type often believing that somewhere in the world lies the perfect pair of glasses and sometime the two will meet, and also believing that almost every sort of bodily disability may be caused by eyestrain. A diagnosis of neurosis is not hard to arrive at, but once it has been made one should be prepared to spend some time with the patient or, if not, to send the patient to some one else who will. One must gain the patient's confidence or no results will be obtained; a hasty, superficial examination will not inspire confidence. Once one is sure of the diagnosis the best procedure is to tell the patient frankly what is the

matter, and explain as simply as possible how the trouble developed. Most people can grasp the fact that the use of the eyes should be a subconscious function, that it is only when we are conscious of them that we suffer from discomfort, and that the only way to get rid of this discomfort is to get the eyes back to the subconscious level. To do this depends largely on the patient's own effort. He should use the eyes, not rest them, and disregard discomfort; when the eyes feel especially uncomfortable they should be used. Such discipline will almost always effect a cure if the patient has confidence in his physician and has what is vulgarly termed "guts."

EDITOR'S ABSTRACT.

DIAGNOSIS OF TUMORS INVOLVING THE SPINAL CORD. H. W. WOLTMAN, J. A. M. A. **95**:1398 (Nov. 8) 1930.

Henry W. Woltman, Rochester, Minn., stresses the fact that the patient's story is the most important step in diagnosis. The earliest and commonest complaint is pain. The pain may be in the spine at the site of the tumor; it may be referred to the lower extremities even when the tumor lies high in the canal, but usually it is referred along the distribution of a posterior root, when it is known as a root pain. Root pains have certain characteristics. They are segmentally distributed; that is, lengthwise in the arms and legs and circularly in the trunk. Then, since tumors grow, the pain becomes more and more intense and adjacent roots become involved; unilateral sciatica becomes bilateral sciatica, and unilateral trunk pain has added to it a complementary pain on the opposite side, completing the so-called girdle. Since there are usually no diseased organs at the site of the pain, there is, as a rule, no local tenderness. Coughing, sneezing, compression of the jugular veins, or, in short, anything which suddenly increases the pressure of the spinal fluid aggravates the pain. Root pains have a habit of awakening the patient from sleep at 3 or 4 o'clock in the morning. He discovers that relief may be obtained by walking, or by sleeping in a chair. In both of these positions the spine becomes relatively shorter. A helpful test consists in flexing the head sharply on the thorax; this simple maneuver often elicits or accentuates the pain. The explanation is probably to be sought in the resulting traction on the cord and dura, and in the increased congestion within the head which displaces the cerebral fluid into the spinal canal. A blue pencil, which Richard Bright referred to as "the most useful instrument of the physician," will be found helpful. It is important to know the precise site of the pain, which may be marked on the patient. The dates of its appearance and its radiation should be recorded. By and by the patient may become aware of clumsiness in running, or of outright muscular weakness. As a rule, the weakness is slowly progressive. Inspection of the tips of the patient's shoes may show a decided difference in wearing. Some patients collapse suddenly, arise, and wonder why they fell; this often happens in case of dumb-bell-shaped tumors which lie partly within and partly without the spinal canal, and may be due to transitory compression of the cord. Other patients who become suddenly weak may have suffered from hemorrhage or softening of the cord incidental to the tumor. Subjective sensory disturbances appear sooner or later. Disturbances in the sphincteric and sexual spheres may add to the discomfort of the patient. Following spinal puncture, aggravation of all symptoms is common; a neurologic examination may then enable one to establish a level of disturbance with ease when it was impossible before. Woltman reports three cases in which tumors were found at different segmental and transverse situations. He discusses the hydrostatic and chemical changes of the spinal fluid, the value of roentgenography in diagnosis and the difficulty often encountered in arriving at a diagnosis. Repeated examinations may be necessary in order to establish a diagnosis. Occasionally exploratory laminectomy is advisable, particularly if progressive involvement of the cord makes further delay perilous. However, exploration without definite indication of the correct level of disturbance is almost certain to result in disappointment.

EDITOR'S ABSTRACT.

DIVERGENT STRABISMUS FROM PERMANENT DISSOCIATED PARALYSIS OF ONE COMMON MOTOR OCULI IN A PARKINSONIAN ENCEPHALITIC. J. ABADIE and E. LAUBIE, Rev. d'oto-neuro-opht. **8**:100 (Feb.) 1930.

Oculomotor troubles are frequent in encephalitis. In the period of invasion they consist of isolated muscular paralyses. Ptosis is the most common, though it is not always due to paralysis, but rather to a diminution of tonus. Strabismus is frequent also, due to oculomotor or, more rarely, to paralysis of the external rectus, but it is dissociated, variable or migratory. Paralysis of function, represented by troubles of associated movements of the eyes, can occur. This is due at times to a simple myasthenia. Nystagmiform jerks are also attenuated equivalents of these paralyses. After the acute phase, the paralyses may be ameliorated or even disappear completely, only to recur suddenly and indicate a recrudescence of the disease. In the waning stage of encephalitis, isolated paralyses of accommodation and nystagmus are rare, although this statement is not confirmed by statistics. Blum remarked that this discordance is due to two errors: variable duration of the paralysis of the stage of invasion, there being no statement as to what stage the paralysis began in, and the affirmation of muscular paralysis on the sole discovery of diplopia, which can be due to a functional trouble, common in the chronic stage.

A woman, aged 31, entered the clinic complaining of trembling of the limbs and muscular stiffness. She had been in good health up to her twenty-fifth year, except for a goiter which had existed from infancy. At this time, being six months' pregnant, she suddenly became diplopic, vision was fogged and there was violent occipital headache; this was followed by a confusional state and insomnia which lasted for eight days, after which she slept profoundly for nine days. In a few days she improved, and three months later, apparently perfectly cured, she bore a healthy child. Three years later, there occurred a divergent squint, which still persists, trembling of the hands and slowness of movements. After two years, difficulty in speech appeared. For the past three months the trembling had been in the lower limbs also, and there had been stiffness of the muscles of the neck. At the time of admission, divergent strabismus of the right eye and a parkinsonian syndrome were noted. Speech was monotonous, the head and neck were held forward and the patient could not turn the head; the arms were in slight flexion, the fingers extended and the thumb in apposition. The tendon reflexes were exaggerated in the legs. The spinal fluid was normal, with a negative Bordet-Wassermann reaction. The right globe of the eye was held in an extreme lateral position; there was no ptosis, but there was an incomplete paralysis of the internal and inferior recti muscles. No functional paralysis of associated eye movements was found. The visual acuity, without correction, was ½ in the right and ⅚ in the left eye; with a lens of —0.75 diopter on the right and a lense of —1 diopter on the left, vision was normal. The eyegrounds were normal.

The ocular paralysis occurred three years after the period of invasion of the encephalitis, at the beginning of the parkinsonian phase, and thus marked a recurrence of the disease. This observation confirms Wimmer's opinion that such ocular complications are rare in the chronic stage of epidemic encephalitis, and that they alone can signify the onset of a new outcropping of the disease and thus indicate the persistence of the infectious encephalitic process.

DENNIS, Colorado Springs, Colo.

THE MYELO-ARCHITECTONIC STRUCTURE OF THE CORTEX OF THE DORSAL TEMPORAL LOBE IN MAN. E. BECK, J. f. Psychol. u. Neurol. **41**:129, 1930.

Beck finds that in man the portion of the temporal lobe lying within the sylvian fissure can be divided into eleven regions and subregions, each of which can be distinguished definitely from the others. Aside from the allocortical fields, which may be said to represent a sort of a foreign body within the temporal lobe, there is found orocaudad a constant increase in the density of the myelin fibers

and of the radii as well as in the number and caliber of the individual fibers. This increase is throughout a graded one, the gradation coexisting with a constant gradual diminution of the structure of the ground fiber network. In spite of these gradations in structure, each area has its own distinctive characteristics by which it can be clearly identified. The margins of the various areas may be seen at one time within a fissure and the next time within the culmen. Fissures almost always indicate a new area, although new areas by no means indicate fissures. The ascending and descending branches of a fissure are almost always similar in structure. At the border line between two fields, one can make out frequently a shallow invagination of the cortex which can be distinguished clearly from the so-called vascular fissures. Beck regards these invaginations as abortive fissures. The mere occurrence of a new field does not necessarily indicate a difference in the structure of its various layers; this applies to regions as well as to subregions.

There seems to be no important quantitative or qualitative difference between the right and the left areas. Nor do there appear any marked qualitative variations in these areas in brains of different persons.

The myelogenic investigations of this part of the brain by Flechsig showed that the anterior part of the transverse convolution was the principal cortical center for hearing. According to Flechsig, this center extended only slightly over to the first temporal lobe at the point where the anterior transverse convolution is invaginated into the temporal lobe. These views coincide with those of Henschen. Beck's investigations also bear this out, because he finds that the anterior transverse convolution consists of an exceptionally well developed cortical area which is the only area in the entire temporal lobe showing an unusually large number of myelin fibers.

A comparison of a reconstruction of the temporal lobe of man with that of the chimpanzee shows that there is no actual difference in the number of regions between the two, although the regio entorhinalis, which in man runs very deeply into the temporal pole, is absent in the chimpanzee. The myelin fiber content, on the other hand, is in the chimpanzee far below that of man; this is especially observed in the ground fiber network which is ever so much richer in man. It is also noteworthy that the Kaes-Bechterew zone and the external margin of the Baillarger zone is more prominent in man than in the chimpanzee. These observations would seem to show that, although there may be no quantitative differences in these areas between man and chimpanzee, the qualitative differences are very marked.

KESCHNER, New York.

CHOREA AND THE LENTICULAR NUCLEUS. NIESSL VON MAYENDORF, Monatschr. f. Psychiat. u. Neurol. **74**:273 (Jan.) 1930.

In this article the author attacks the current theory that certain changes in the putamen are directly associated with the choreic syndrome. His main arguments are drawn from a case of postapoplectic chorea of embolic origin in a woman, aged 23. The duration of the illness was seventeen years. The choreic movements were limited mainly to the left upper extremity, but sometimes spread to the left leg. During emotional outbursts, they also involved the right side. The tendon reflexes were increased on the left, and there was a hemihypesthesia with partial tactile agnosia on that side. The mental symptoms strongly resembled the picture of Huntington's chorea. Anatomically, the case was investigated by staining the myelin sheaths, serial sections of the whole brain being made. The main lesion was a large softening in the right supramarginal region. It extended forward, however, underneath the middle portion of the postcentral convolution. Secondary degeneration was observed in a tract which ran from the softening through the posterior portion of the lenticular nucleus. The further course of these fibers could not be ascertained definitely. Two alternatives were considered: either they joined the posterior and outermost portion of the posterior limb of the internal capsule, thence running in the pyramidal tract, or they reached the lemniscus in which they dispersed, connecting up finally with the posterior

columns. There were other smaller softenings, but none of them involved the corpus striatum or the red nucleus. It was noted that some fibers in the middle cerebellar peduncle showed secondary degeneration. As this possibly indicated an interruption of corticocerebellar impulses, it would tend to support the old theory that chorea was due to a cutting off of the cerebellum from the cerebrum. The author believes, however, that the choreic symptoms in this case owed their origin to the destruction of the first mentioned group of fibers. He agrees with Wilson that the choreic movements occur as the result of a disturbance of the function of the pyramidal tract produced by the falling out of certain sensory stimuli. In his case this was caused by the softening which extended underneath the postcentral gyrus. In support of his view that the choreic syndrome is not due to the activity of subcortical motor mechanisms, he mentions the fact that choreic movements are never observed when the pyramidal tract is completely interrupted. As further proof he reports three cases in which there were no choreic or other extrapyramidal manifestations in spite of the fact that they all showed lesions of the putamen on one or both sides. Hence the author is inclined to doubt the correctness of the prevailing dogmas concerning the so-called striatal diseases. He believes that the most important conclusion to be drawn from his work is that the putamen plays no part in the production of the choreic syndrome.

The article contains a wealth of additional data concerning the paths taken by other fibers and tracts. These observations are of considerable interest, but do not lend themselves well to abstracting.

ROTHSCHILD, Foxborough, Mass.

TUMORS OF THE RHINOPHARYNX WITH CRANIAL PROPAGATION: THEIR EARLY DIAGNOSIS AND THE IMPORTANCE OF ROENTGENOLOGIC EXAMINATION. G. WORMS and R. CARILLON, Rev. d'oto-neuro-opht. **8**:161 (March) 1930.

Six well studied and fully reported cases prompted this article. When tumors of the rhinopharynx begin in the peritubal region they rarely show characteristic signs of their presence. The patient usually exhibits an ordinary pharyngitis until some complication arises, which is almost always a disease of a nerve. These tumors grow by preference toward the skull along the course of the eustachian tube and enter the cranial cavity by erosion of the bone rather than by infiltration or by way of the basal foramina. Paralysis of the trigeminus is an early sign, beginning with pain, which is of moderate severity and is continuous. The superior and inferior maxillary divisions are affected before the ophthalmic and are tender to pressure over their points of emergence. The motor fibers participate in the disturbance, indicated by atrophy of the masticator muscles and by an oval oblique shape of the mouth, caused by projection of the inferior maxilla toward the healthy side.

Great stress is placed on the value in diagnosis of careful roentgenologic studies of the cranial base. According to Hirtz' technic, the tube must be centered exactly over the petrosphenoidal region of the suspected side. Loss of detail of the structure of the point of the petrous pyramid, veiling of foramina in the middle fossa and abnormal transparency of the bony mass eroded by the neoplasm may be seen. At a later stage, a distinct lacuna, usually limited behind by the superior crest of the pyramid, will be found. Sometimes the shadow of the tumor in the nasopharynx can also be made out.

In the early stages, enlarged retromaxillary or submaxillary (angle) glands may be felt, and at times they are even found on both sides.

Subcranial neoplasms, which arise from the mucosa or the adjacent lymphoid structures, are epitheliomas or lymphosarcomas, while those arising in the bone or degenerated dura are osteosarcomas, fibrosarcomas, psammonas, meningiomas, etc.

To the trigeminal paralysis is soon added paralysis of the abducens nerve, and the syndrome of the petrosphenoidal junction is complete. Later on, the syndrome of the cavernous sinus develops. More rarely the posterior fossa is invaded and facial, vestibular and pontile symptoms appear. In one of the cases the facial

nerve was paralyzed from erosion and extension of the tumor into the tube, the middle ear and its adnexa. The anterior fossa is still more rarely invaded. The anosmia complained of is caused by mechanical obstruction of the nares.

Extension of the growth laterally results in bilateral paralysis. In one case both fifth and sixth nerves were involved. The spinal nerves are almost always spared, although in one case paraplegic phenomena were explained by a vertebral metastasis. Exceptions to the rule that these tumors do not cause increase of intracranial pressure were found in two cases, for both showed papillary stasis and one required decompression. Involvement of the sinuses, orbit and nasal fossae is a terminal phenomenon. Death occurs in from six to twenty-four months.

DENNIS, Colorado Springs, Colo.

NARCOSIS AS THERAPY IN NEUROPSYCHIATRIC CONDITIONS. W. J. BLECKWENN, J. A. M. A. **95**:1168 (Oct. 18) 1930.

W. J. Bleckwenn, Madison, Wis., asserts that sodium iso-amylethyl barbiturate, used according to the method advocated, will induce narcosis in the various types of excitement and benign depression and in the convulsive states. Periodically induced narcosis is decidedly beneficial in neuropsychiatric cases, simplifying the management and materially shortening the course of the illness. Normal lucid intervals, with spontaneous speech and the taking of nourishment, are seen in protracted cases of catatonic schizophrenia. Periodic narcosis breaks down the stubborn insomnia associated with the more severe psychoneuroses. For therapeutic purposes in the types mentioned, a certain method and technic of administration is essential. This consists of (1) dosage; (2) dilution of drug; (3) rate of intravenous injection; (4) depth of narcosis. Bleckwenn has found the following technic successful: The patient should have no food for from four to six hours preceding the administration of the drug. The drug is freshly dissolved in triple distilled water. A 5 per cent solution is made. Each cubic centimeter thus contains three-fourths grain of the drug. The drug is injected intravenously at a rate not to exceed 1 cc. per minute. It is necessary to use a watch for this, since it is extremely difficult to inject accurately from 10 to 20 cc. over a period of from ten to twenty minutes without the hesitating, jerky type of injection. The initial dosage is individual and for neuropsychiatric cases it is absolutely safe to give 2 cc. (1½ grains) more than is necessary to produce corneal anesthesia. He uses the abolition of the corneal reflex as the criterion of proper narcosis and gives an additional 1½ grains. The average neuropsychiatric patient will thus receive between 7 and 15 grains intravenously. This is approximately half the amount used for surgical anesthesia. In only one case has it been found necessary to exceed 15 grains in order to produce the required narcosis. This was in a woman who had received more than 250 injections during a period of nine months. It gradually became necessary to increase the dose to 21 grains. There seems to be a slight increase in the tolerance for the drug after prolonged use. The drug may be used intramuscularly, in which event the dosage is increased and the solution is more concentrated. A 20 per cent solution is prepared, and of this Bleckwenn gives from 2.5 to 5 cc. or from 10 to 20 grains. By the intramuscular route a narcosis is produced, but this is slower in its development and less profound, as compared with the response to the intravenous method. In mild cases the drug can be used orally in doses of from 3 to 6 grains. It takes about forty-five minutes to be effective. It is effective as a hypnotic in the less severe types and is ineffective in the disturbed and violent cases. And, finally, the patient must always be watched by a nurse from the time of administration of the drug until the initial narcosis wears off. This precaution is advisable because of the dangers of aspiration of vomitus and, further, because of the depth of narcosis and possibilities of suffocation. If this method of administration is followed, observing the factor of greater dilution and measured rate of injection, the occasionally embarrassing reactions of greatly lowered blood pressure and shallow respiration are avoided.

EDITOR'S ABSTRACT.

ACUTE ANTERIOR POLIOMYELITIS IN CALIFORNIA. EDITORIAL, J. A. M. A. **96**:117 (Jan. 10) 1931.

Certain epidemiologic characteristics of acute anterior poliomyelitis are apparently well established, yet the nature of the virus remains unknown. Moreover, the reports of the prevalence of this disease indicate, at least in California, that it is continually spreading with the occurrence of outbreaks in fairly short intervals, namely, 1925, 1927 and 1930. The method of propagation, however, remains an enigma and offers a distinct challenge to public health authorities. One of the important phases of the disease which make it difficult to recognize and control is the number of abortive cases that must occur in any epidemic. The contagiousness is exceedingly low, the latent immunization of the general public exceedingly high, or the carrier produced by contact to cases of comparatively little moment in the spread of the disease.

According to the figures of the California State Department of Public Health, the outbreak in California in 1930 began to be statistically manifest early in May, the curve rising rapidly to a peak in July (95 and more cases being reported daily), a sharp drop in August (60 and less cases being reported daily) with a gradual climb to a second peak in October (85 or more cases being reported daily) with an abrupt decline in November, 1,707 cases being reported for the period of ten and a half months. The curve of the 1925 outbreak, 821 cases, reached its peak in July, with a sharp decline in August and September and a gradual leveling off, with a small uplift in November. The curve of the 1927 outbreak, 1,298 cases, had a series of peaks in July, in August and in September, with a small uplift early in November. Two centers of population suffered most, Los Angeles and San Francisco, in the outbreak for 1930. The second peak in the curve for 1930 probably represents the San Francisco outbreak, for cases began to be reported there much later than in Los Angeles. Curiously, only a small number of cases were reported in Oakland, just across San Francisco Bay. The age incidence for 1930 presents some interesting data. For instance, 334 cases were reported between the age limits of 15 and 35, approximately 20 per cent of the total; 1,000 cases between 0 and 10 years, 301 from 10 to 15; 35 from 35 to 45; 10 from 45 to 55; 3 over 55 and the remainder classified as adult unknown or, at present, in doubt. The George Williams Hooper Foundation for Medical Research of the University of California, which distributed convalescent poliomyelitis human serum, reports that during the period of June 1 to Dec. 1, 1930, more than 19,750 cc. was given to physicians and institutions for administration to patients; 10,650 cc. of serum was given to physicians in San Francisco County alone. The number of donors was 202, and 38 were bled twice and 9 three times during the epidemic period.

It is, indeed, fortunate that research institutions have taken up the burden of supplying convalescent poliomyelitis human serum, since this important health department activity has been quite neglected though Netter advocated its use in 1910. The value of such serums is apparently well established and of practical therapeutic importance even in the absence of controls. The prophylactic use of convalescent serum for susceptible contacts cannot be advocated until the supply can meet the drastic needs of epidemic periods. EDITOR'S ABSTRACT.

A CASE OF OTOGENOUS TOTAL OPHTHALMOPLEGIA (CONTRALATERAL). M. S. ROSENBLATT, Rev. d'oto-neuro-opht. **8**:523 (July) 1930.

A girl, aged 16, complained of violent headaches, pain in the neck on turning the head, repeated vomiting, chills and fever, and pain in the left ear, which had discharged since infancy. Examination revealed a poorly nourished girl, apparently suffering greatly, with subicteric color of the skin and sclera. The temperature was 40.2 C. (104.3 F.); the pulse rate was 120; the heart and lungs were normal; pressure over the left mastoid and the sternoclavicular joint was painful. The left ear was filled with fetid pus; the drum membrane was destroyed, and the tympanum was filled with granulations. Hearing in the left ear was greatly reduced. The cranial nerves showed no disturbances. The right patellar reflex

was slightly exaggerated. The leukocyte count was 16,875; no eosinophils were present; stabs, 19.5 per cent; segmented, 62.5 per cent; lymphocytes, 9 per cent, and monocytes, 9 per cent.

An operation on the radical mastoid, performed on the next day, revealed a fistula in the bone, filled with pus and granulations, which proceeded from an abscess in the sigmoid sinus to the surface of the bone; the middle ear was filled with granulations and cholesteatoma, and the tegmen of the antrum and tympanum was softened and was removed. The infected thrombus in the jugular bulb necessitated an extensive resection of the bone and ligation of the jugular vein. A second operation, one week later, uncovered a collection of pus around the jugular bulb and softened bone around the lateral sinus. Improvement followed for a week and then vomiting, diplopia and pain in the right eye and temple appeared, accompanied by an increase of leukocytes in the blood. The pains in the eye continued for a week. The ophthalmoplegia began with the abducens and the levator of the lid, and progressed until there was complete paralysis of all of the ocular muscles, including the pupil. This condition persisted for about one month when improvement began which progressed until complete restitution of the function of the eye was attained—a period of seventy-five days. At the time of the appearance of the paralysis of the abducens muscle Babinski and Gordon signs were present on the right. The Wassermann reaction of the blood was negative.

The phenomenon of an ophthalmoplegia on the right resulting from an otogenous infection on the left is explained by the transference of the infection by means of the blood vessels: from the left jugular bulb through the left inferior petrosal sinus, basilar plexus and the right petrosal sinus to the point at which the latter joins the cavernous sinus. This produced edema in the basal meninges and perhaps a circumscribed meningitis also at the point of the petrous pyramid, at which the oculomotor nerves and the gasserian ganglion are close together, and resulted in a neuritis of these structures. The assumption is that the virus was much attenuated.

DENNIS, Colorado Springs, Colo.

EXPERIMENTAL STUDIES ON THE DEVELOPMENT OF THE EYE. III. THE EFFECT OF THE SUBSTRATE ("UNTERLAGERUNG") ON THE HETEROTOPIC DEVELOPMENT OF MEDIAN AND LATERAL STRIPS OF THE ANTERIOR END OF THE NEURAL PLATE OF AMBLYSTOMA. HOWARD B. ADELMANN, J. Exper. Zool. **57**:223 (Oct.) 1930.

The influence of the substrate on the eye-forming potencies of median and lateral thirds of the anterior end of the neural plate of *Amblystoma* was tested by transplantation of the strips with and without substrate to the belly walls of older hosts. Only 11.1 per cent of 90 transplants of lateral strips without substrate developed well formed eyes, while 54.4 per cent of 145 transplants of lateral strips with substrate formed eyes. The substrate evidently reinforces the eye-forming potencies of the lateral regions of the neural plate. In the case of median strips, 70.8 per cent of 89 transplants without substrate developed well formed eyes, while 72.6 per cent of 113 transplants with substrate formed eyes. The eye-forming potencies of the median third of the neural plate are therefore higher than those of the more lateral areas. While the substrate in the stages considered has very little, if any, "reinforcing" effect on the eye-forming potencies of the median strips, it may possibly have exerted such an effect in stages earlier than those used.

The substrate does have an interesting effect on the character of the eyes formed from the transplanted median strips. Two distinct eyes separated by ventral brain floor were formed in 47.6 per cent of eighty-two transplants of median strips with substrate, while no such cases were found in those without substrate. In addition, 23.2 per cent of the transplants of median strips with substrate formed two eyes, one of which was rudimentary. In sixty-three transplants of median strips without substrate, 73 per cent formed perfectly single

eyes resembling cyclopean eyes in their relations to the implanted brains. It is concluded that the substrate is responsible for the bilateral character of the development of the eyes in the transplants of median strips with substrate.

A case is described in which the donor formed an eye from a right lateral third of the anterior end of the neural plate left in situ, while eyes were formed from both the median and left lateral strips of the anterior end of the neural plate from the same donor when transplanted to older hosts. The evidence indicates that the eye-forming materials of the neural plate alone constitute a harmonic equipotential system capable of forming either one eye or two eyes, according to the conditions of development. While the eye-forming materials of the neural plate alone constitute a potential unit, it is not correct to say that a single median eye is present in the early neural plate. Although eye-forming potencies of the neural plate alone are higher in the median regions, the evidence of excision and staining experiments points to the conclusion that during normal development more lateral regions are also involved in the development of the eyes.

WYMAN, Boston.

SHRINKAGE OF THE BRAIN EMBEDDED IN PARAFFIN. S. A. SARKISSOW, J. f. Psychol. u. Neurol. **41**:76, 1930.

A proper evaluation of the results of cyto-architectonic investigations of the brain can be aided greatly by determining: (1) the effect of formaldehyde, alcohol, chloroform and paraffin, respectively, on the volume of brain substance; (2) the changes, produced by cutting and mounting, in the size of sections embedded in paraffin; (3) the coefficient of shrinkage or of swelling following the various technical methods of preparing the sections. This study was undertaken by Sarkissow to obtain the necessary data for the determination of these three questions. His conclusions may be summarized as follows: 1. There always occurs a certain amount of swelling of the brain while it is kept in paraffin. 2. A difference of from ten to twenty-five days, in keeping the brain in chloroform, has no actual effect on the further progress of swelling or of shrinkage. 3. Shrinkage of blocks of the cerebral hemispheres occurs chiefly in solution of from 60 to 70 and 80 per cent alcohol; very little shrinkage results from a solution of 90 per cent alcohol, and practically none from absolute alcohol. 4. Chloroform produces a certain amount of swelling of the brain. 5. Blocks kept in paraffin undergo a certain amount of shrinkage, which is, on an average, from 8 to 10 per cent of its "chloroform" size. 6. Linear measurements of the sectioned surfaces of the blocks show a variation in the degree of shrinkage in each individual block, differing according to the direction of the sectioning; there is also a variable "average degree" of shrinking of the various blocks, so that the nearer the sections are to the frontal pole, the greater is the shrinkage. 7. The manifestations of shrinkage also vary in different brains. 8. In comparison to the cortex, there is considerably less shrinkage of the white substance. At the same time, the percentage of shrinkage of the cortex as well as of the white substance varies in different blocks and in different brains. 9. As compared with the corresponding cut surfaces of the blocks, there occur certain changes in the size and shape of the sections while they are being cut and mounted. Staining of previously mounted sections has no effect on the size of the sections. 10. In order to obtain sections of as uniform a size as possible the human brain must be sectioned and brushed in the dorsoventral direction. The use of parchment paper is to be preferred to brushing. 11. The coefficient of linear shrinkage (measurements of the convolutions and of sections of blocks) lies between 1.2 and 1.24. 12. For the restoration of the surface content of any one architectonic field in its "formaldehyde size," every section of the thickness of 20 microns must be regarded as being 28 microns in thickness. 13. A uniform technic in the preparation of the material is absolutely essential for the proper solution of individual, racial and other architectonic problems.

KESCHNER, New York.

IMMUNIZATION STUDIES IN POLIOMYELITIS. CURRENT COMMENT, J. A. M. A. **96**:119 (Jan. 10) 1931.

Poliomyelitis, or infantile paralysis, is no longer classed as a rare disease. The management of poliomyelitis and its consequences has made considerable progress, thanks to persistent scientific investigation. The possibility of direct transfer from person to person seems to be well established. Today, most investigators are convinced that poliomyelitis is caused by one of that still vague category of agents, the filtrable viruses. Furthermore, the discovery by Flexner and Lewis and by Levaditi and Landsteiner in 1910 that the serum of patients convalescent from an attack is capable of neutralizing the filtrable virus has been of the greatest importance. According to Park (In Jordan and Falk: Newer Knowledge of Bacteriology and Immunology, Chicago, University of Chicago Press, 1928), the serum from slight abortive cases is, on the average, as potent as that from pronounced cases. The serum of many persons who have never had poliomyelitis contains antibodies, but these are not so potent as in the serum of convalescent cases. The antibodies remain for a long time in the blood of persons who are convalescent. It is well known that a variety of viruses can be absorbed and rendered ineffective by a number of colloidal and particulate chemical substances. Rhoads (Immunization with Aluminum Hydroxide Mixtures of Poliomyelitis Virus, *Science* **72**:608, 1930) of the Rockefeller Institute for Medical Research, New York, has recently discovered that poliomyelitis virus can be inactivated by suspensions of aluminum hydroxide. This reaction is promoted in an acid medium and may be prevented by an alkaline environment. The striking feature, however, is the demonstration that the virus, when adsorbed on aluminum hydroxide, is incapable of producing poliomyelitis but still capable of inducing active immunity in *Macacus rhesus*. In a small series of animals thus immunized, symptoms of experimental poliomyelitis did not appear and in only one was the degree of immunity, although adequate to protect against nasal instillation, insufficient to protect against intracerebral injection of virus. Intracerebral inoculations of the aluminum suspension alone were without pathologic effect. The mere recital of these experiments offers a bright prospect of helpful possibilities in the attack against infantile paralysis. It has depended, and will continue to depend, on animal experimentation. This may well be stressed at a time when opponents of experimentation on animals are making vigorous efforts to prevent such studies as are destined to assist in averting one of the most pathetic blights of child life.

EDITOR'S ABSTRACT.

THE PULMONARY SYNDROMES OF LESIONS OF THE SPINAL CORD. L. CORNIL, A. HAMANT and M. MOSINGER, Ann. de méd. **28**:453 (Nov.) 1930.

The effect of lesions of the spinal cord on the vegetative regulation of the lungs was studied in eight cases. According to the pulmonary syndromes the cases were divided into three groups: early posttraumatic lesions, complicated recidival lesions and progressive infections. In 50 per cent of the patients the residues of healed pulmonary disease were found; it seems probable, therefore, that the scars were the starting points of pulmonary disease following sympathetic dysfunction with abnormal vascular reflexes.

Marburg and Ranzi emphasized during the war the interrelationship between laminectomy and pulmonary disease, and their observations were confirmed in 1923 by Martel and Clovis Vincent. Congestion and edema of the lungs may follow laminectomy while the patient is still on the operating table and may bring about early death. In addition, intense abdominal vasodilation is often found, a combination similar to that found after lesions of the spinal cord have occurred. In ascending forms of acute myelitis or in myelopathies, a sudden pulmonary congestion develops at the moment when the disease process invades the upper segments of the spinal cord.

The following facts are cited in order to prove that the pulmonary disease developing immediately after laminectomy or lesions of the spinal cord is primarily

not of infectious origin, but is produced by disturbances of the sympathetic innervation. The pulmonary symptoms are similar to those that follow lumbar or cervical sympathetic ramisectomy or cervical gangliotomy. A cervical ramisectomy performed for the relief of trophic disturbances of the left hand was soon followed by congestion and bronchial exudation in the left lung. The expectoration contained numerous eosinophilic cells. In two lumbar ramisectomies for the relief of trophic disturbances of the right leg, an abdominal vascular congestion and bronchial expectoration followed after five days. Sympathectomies which spare the stellate ganglion are not followed by pulmonary complications, while on the other hand the extirpation or irritation of this ganglion may give rise to an acute pulmonary edema.

The bronchopneumonia that follows lesions of the spinal cord may be of either the acute or the chronic type. In both, the pulmonary vasodilatation with minute hemorrhages and bronchial hypersecretion are predisposing factors that favor the growth of the micro-organisms responsible for the ensuing infection.

WEIL, Chicago.

INCIDENCE OF BROMIDE INTOXICATION AMONG PSYCHOTIC PATIENTS. C. P. WAGNER and D. E. BUNBURY, J. A. M. A. **95**:1725 (Dec. 6) 1930.

Since March, 1928, a determination of the bromide content of the blood serum has been a part of the routine in the examination of all patients admitted to the Colorado Psychopathic Hospital. Carl P. Wagner and D. Elizabeth Bunbury, Denver, have made a study of the first thousand consecutive cases so examined. Of the thousand cases examined, 7.7 per cent showed bromide in the blood serum in a concentration of 75 mg. per hundred cubic centimeters and over. Of these, thirty-three, or 42.85 per cent, had received the bromide on a physician's prescription; fourteen, or 18 per cent, had taken "patent" medicines; and in thirty, or 38.95 per cent, the source of the drug remained undetermined, but undoubtedly these patients had also taken "patent" medicines, although most of them denied that they had taken medicine of any kind, even when they were confronted with the fact that their illness was due to drug intoxication. In seventeen, or 22.08 per cent, admission to the hospital was sought entirely on account of drug intoxication. Most of these patients recovered before or shortly after leaving the hospital. However, two cases terminated fatally, and in these death was due to the indiscriminate use of bromides only. Both of these patients showed a bromide concentration of over 300 mg. per hundred cubic centimeters of blood. On admission, both had been under the care of a physician and had been taking bromide on prescription. Five other cases terminated fatally. One of these, a patient with dementia paralytica, showed only 75 mg. per hundred cubic centimeters, and the authors do not believe that the bromide contributed toward his death. The four remaining patients, one with cerebrospinal syphilis, one with senile dementia, and two with cerebral arteriosclerosis, died of cardiac decompensation. In these the bromide contributed toward their death in that the excitement due to delirium aggravated the decompensation. The authors assert that undesirable mental symptoms can be reduced to a minimum if the physician will be on the outlook for exacerbation of mental symptoms during bromide administration or if he is willing to make determinations of bromide concentration in the blood. Special care should be exercised in the administration of bromide in cases of organic nervous disorders, particularly those in which the excretory or circulatory functions are impaired.

EDITOR'S ABSTRACT.

THE PATHOLOGY OF MEASLES ENCEPHALOMYELITIS. J. G. GREENFIELD, Brain **52**:171 (July) 1929.

Greenfield believes that it is necessary, for descriptive purposes, to separate a cerebral from a spinal form of encephalomyelitis following measles, although they are often combined. The cerebral form usually appears with a recrudescence of

fever, in which somnolence or delirium and often convulsions are manifested. In almost every case the patient is soporous or even comatose. Definite signs of meningitic involvement are present. Papilledema is fairly common, and temporary amaurosis has been observed. This somnolent stage may pass off in a few hours, but can last a few days. A state of instability follows which is characterized by choreiform movements, or by naughtiness and bad temper. The patients usually recover from this stage in a few days, although a change in character can continue permanently. Cerebral or cerebellar focal sequelae may develop, but they are uncommon. The spinal type may be ushered in during a recrudescence of fever, but this does not always occur. Paralysis is usually confined to the lower half of the body and is associated with loss of sphincter control. As a rule the paralysis is flaccid, but tends to become spastic after the first forty-eight hours, with increase of deep reflexes and an extensor type of plantar response. The paralysis may be accompanied by a dissociated anesthesia in which pain and temperature sense is disturbed while touch remains intact. On the whole, examination of the cerebrospinal fluid is valuable only as a means of excluding other diseases rather than giving conclusive evidence of the presence of encephalomyelitis. Recovery, when it occurs, is usually remarkably complete. It is evident, therefore, that encephalomyelitis that occurs in some convalescent cases of measles must be regarded as a disease entity, distinct from epidemic encephalitis or Landry's paralysis.

The pathologic changes may be of three main types: (1) diffuse congestion of the brain, especially of the white matter, sometimes causing petechial hemorrhages, (2) discrete round cell, perivascular infiltration and (3) small unmistakably characteristic zones of demyelinization.

Neither clinical nor pathologic distinctions could be drawn between encephalomyelitis following measles and that which may follow vaccination for smallpox, while the epidemiologic incidence supports the similarity of the two diseases. It is therefore probable that these two conditions are caused by an unknown virus which spreads in epidemic waves, but which produces no disease unless stimulated to activity by the exanthematous disease.

BECK, Buffalo.

THE INFLUENCE OF THE NERVOUS SYSTEM IN THE REGENERATION OF EISENIA FOETIDA SAVIGNY. PERCY LAURANCE BAILEY, JR., J. Exper. Zool. **57**:473 (Nov. 5) 1930.

When the nerve cord of *Eisenia foetida* is cut in two, no coordinated movements occur involving both the anterior and the posterior parts of the worm until the cut ends of the cord have become united by nerve fibers. These fibers grow out from the cut ends of the cord, through the cicatrix plug, sometimes bridging the gap after forty-eight hours. When the cut is through a ganglion, nerve cells of the ganglion adjacent to the wound probably migrate or are pulled into the region of the wound by some mechanical force, such as tension of the cicatrix. These cells help to form the new ganglion. When one or more ganglia are removed from the cord the same process of repair takes place, although the time is much greater before the gap is bridged and before coordinated movements reappear. Because of the fact that coordinated movements do not occur until it can be demonstrated that nerve fibers have completely bridged the gap in the nerve cord, it is probable that the nerve cord alone carries the impulses which are responsible for coordinated movements.

Anterior pieces of normal worms cut in two at the region posterior to the clitellum begin to regenerate a new posterior end after from seven to twelve days. The regeneration takes place more rapidly in summer than in the colder winter months. There may be a seasonal variation in the rate of regenerative processes. When the nerve cord of *Eisenia* is cut in two and the cut ends are looped back on each other, leaving a space of several segments in which no nerve tissue is present, the cut ends become mingled with the muscle and connective tissue of the wall of the body. No regeneration of fibers is apparent. If the animal is cut in two through the middle of a region in which there are no nerve elements, but in which the cut ends of the cord have been looped back, impulses do not

travel from the region of the cord to the cross-cut region of the wound. The anterior pieces of worms so cut do not regenerate at the posterior end. Occasionally, the looped cord slips back into its natural position before the second operation. In these cases regeneration, either normal or abnormal, may take place. No cases of regeneration were observed when the nerve cord remained looped back several segments from the cut surface or when the nerve cord was not present at the cut surface.

WYMAN, Boston.

MIGRAINE. C. J. BARBORKA, J. A. M. A. **95**:1825 (Dec. 13) 1930.

The fifty patients reported on by Clifford J. Barborka, Rochester, Minn., have been on the ketogenic diet from three to thirty-six months. For purposes of study the cases have been tabulated in three groups: (1) those in which the attacks of migraine have been controlled by the ketogenic diet; (2) those in which there has been definite improvement by lessening of the frequency or severity of the attacks, and (3) those in which the treatment failed. The age of the patients varied from 16 to 66 years; the period over which attacks of migraine had occurred varied from four to fifty-four years prior to the time of treatment. Fourteen of the fifty patients controlled the migraine by the use of the ketogenic diet. The cessation of the headaches varied from the time ketosis developed to as long as three months. Most of the patients in this group maintained constant ketosis; a few experienced temporary disappearance of ketosis for a few days. The patients in this group have been on the diet from seven to thirty-six months. Twenty-five patients have been definitely benefited; the attacks of migraine are less frequent and less severe. Only two patients maintained ketosis; the remainder were periodically in ketosis. The migraine of some of the patients in this group was controlled for the time they were in ketosis, and when they broke the diet, recurrence of the migraine followed. Eleven patients did not derive any benefit from the procedure. These patients made an effort to follow the diet from three to six months. Two patients maintained ketosis constantly, but without influence on the attacks. Four patients were in ketosis periodically, and the remaining patients did not reach the state of ketosis. It should be noted that in the fourteen cases in which the attacks were controlled, diacetic acid, tested for daily, was always present in nine cases, and was present intermittently in five. In the twenty-five cases in which the condition was improved, ketosis was maintained in only two, and in twenty-three it was periodic; the diet apparently produced a state of threshold ketosis. Of the eleven patients who were not benefited, only two maintained the diet accurately and were in a state of ketosis, and this was for four months only; they became discouraged because of not receiving benefit and discontinued the diet. Four of the eleven patients were periodically in ketosis and five did not reach this state at any time.

EDITOR'S ABSTRACT.

ASYMPTOMATIC NEUROSYPHILIS. J. E. MOORE and H. H. HOPKINS, J. A. M. A. **95**:1637 (Nov. 29) 1930.

Data regarding the outcome of 123 patients with asymptomatic neurosyphilis (including 55 whose diagnosis on admission was early, and 68 late, syphilis) observed over an average period of seven years are presented by Joseph Earle Moore and H. Hanford Hopkins, Baltimore. Conclusions are based on repeated clinical and spinal fluid reexaminations. The patients are classified in three groups (1, 2 and 3) on the basis of the intensity of the spinal fluid changes. They found that spontaneous regression to normal of positive spinal fluid observations of any degree of intensity is a rare phenomenon. Of 14 patients with group 1 spinal fluids, 6 are clinically and serologically well, 2 have developed clinical neurosyphilis and in 6 the present status is questionable. Of 73 patients with group 2 fluids, 50 are clinically and serologically well, 5 have developed clinical neurosyphilis (of whom 2 developed dementia paralytica and 1 tabes), and in 18 the present status is questionable. Of 36 patients with maximal (group 3) fluid

changes, only 10 are well. Twelve have developed clinical neurosyphilis (of whom 7 developed dementia paralytica and 3 had tabes), and in 14 the present status is questionable. The presence of a group 3 spinal fluid, early or late in the course of syphilitic infection, is strong presumptive evidence of liability to the development of parenchymatous neurosyphilis. Since the average observation period is short, it seems certain that the figures given for the incidence of clinical neurosyphilis are minimal and that from the 38 patients now classified as "status questionable" further examples will develop. Eleven patients of the series are dead, of whom 5 died of neurosyphilis. The authors conclude that the presence of a positive spinal fluid in patients with early or late syphilis who show no objective neurologic abnormalities is of grave prognostic import. Generally speaking, the ultimate danger to the patient is roughly proportional to the intensity of the spinal fluid changes. On the other hand, a negative spinal fluid in early or late syphilis is, subject to certain qualifications, a practical guarantee of safety for the future so far as the development of neurosyphilis is concerned. These facts being true, routine spinal puncture is an indispensable part of the management of every patient with syphilis.

EDITOR'S ABSTRACT.

FAMILIAL NEUROSYPHILIS. C. C. DENNIE, J. A. M. A. **95**:1571 (Nov. 22) 1930.

Charles C. Dennie, Kansas City, Mo., says that with the exception of locomotor ataxia there is no evidence that there is any special neurotropic strain of *Spirochaeta pallida* transmitted from the parents to the children. This statement is supported by the following facts: In the most severe type of all these diseases, dementia paralytica, the father does not transmit his neurosyphilis to the children through the mother. It is perfectly possible for a father and mother who have no evidence of neurosyphilis to transmit a syphilis to their children that will eventually transmute itself into dementia paralytica or tabes and that will affect only one child. Furthermore, parents who have neurosyphilis or other types than dementia paralytica or tabes may transmit, and often do transmit, syphilis to their offspring in this peculiar manner: the oldest child dies of dementia paralytica and none of the other children have neurosyphilis. In familial neurosyphilis it cannot be proved that a neurotropic strain of *Spirochaeta pallida* is transmitted, excepting in tabes dorsalis. The records of a number of families are presented. Dennie says that a general view of familial neurosyphilis impresses the investigator with its tragic hopelessness. While the patient with dementia paralytica does not as a rule transmit neurosyphilis to his offspring, his heritage of inferior mentality and substandard physique is almost as bad. The neurosyphilitic children of tabetic parents respond to treatment, and one is apparently able to arrest the progress of the disease, but their whole life will be hampered by treatment and limited by observation. And, while they would have died without treatment, they will probably become perpetual charges of society because their treatment has been half-way successful. The treatment of children with neurosyphilis presents as many difficulties as the management of adult syphilis of the same type. The ingenuity of the therapeutist is taxed to the utmost. In the last year malaria has been added to the armamentarium and with decided success. It can be used in any child over 1 year of age. The procedure is fraught with danger and one must be constantly on the alert to terminate it.

EDITOR'S ABSTRACT.

NEUROFIBROMATOSIS OF RECKINGHAUSEN'S AND OF PAGET'S DISEASE. A. AUSTREGESILO and D. DO COUTO, Encéphale **25**:592 (Sept.-Oct.) 1930.

The authors first discuss Recklinghausen's disease, pointing out that it is a condition neither very common nor very rare. Over a period of several years, da Fonseca observed twenty-five cases in Rio de Janeiro. After reviewing the classic symptoms, Austregesilo and do Couto discuss the proposition of neurofibromatosis representing a transition between pathology of the nervous system

and of the integument. It seems certain that the vegetative nervous system plays a rôle, since varied signs of the endocrine and sympathetic systems often occur: bronzing, thyroid and suprarenal pictures, asthenia, fatigability, nervous depression, intellectual deficit, etc. Whether these are causes or effects is not clear. Proof exists that, in addition to cases of pure involvement of the terminal nerve, the fibrous tissue of vessels and cutaneous glands often participates. In fact, pure neuromas are rare. The number of tumors occurring on one body may, at times, be prodigious; Smith reported one case with 2,450 discrete masses; Jonseca one with 5,594; Profeta one with more than 7,000. Symptoms are dependent largely on location, with resulting phenomena of nerve pressure. Blockage of the spinal canal occurs.

The authors then discuss the situation existing in Paget's disease, another condition of obscure etiologic nature. Its origin may be very complex, and it is believed necessary to invoke a mixed theory: endocrinosympathetic and arterial. Such a theory can explain the association of Paget's disease with several other disturbances of the endocrine system, e. g., acromegaly, thyroiditis, trophic lesions of the bone and the like. A case is presented of a white woman, aged 68, with two huge facial mollusca and numerous tumors on the body. In addition, the long bones in places manifested the deformations characteristic of osteitis deformans. It seems necessary, thus, to think of the two simultaneous pathologic conditions as of dysendocrine-vegetative origin, and by this point of view light may be shed on both conditions.

ANDERSON, Los Angeles.

MONGOLISM AND ITS TREATMENT. WALTER TIMME, Bull. Massachusetts Dept. Ment. Dis. **14**:229 (April) 1930.

The skeletal disproportions, disturbances in the optic nerves and genital abnormalities so often found in mongolian idiocy suggest a pituitary factor. Roentgenograms frequently support this contention, as many pictures of the skull of persons with mongolian idiocy show high arched anterior clinoids with evidence of enlargement of the anterior chamber of the sella. In forty-five of sixty unselected cases, Timme reports that roentgen study showed a space under the anterior clinoids communicating with the pituitary fossa. He states further, however, that this observation occurs in normal children as well, although it is especially common in mongolian idiots.

With so much evidence of endocrine dysfunction, rational therapy, Timme believes, demands glandular treatment. Since 1920, he has been giving mongolian idiots anterior lobe pituitary substance (2 grains [0.13 Gm.] daily), whole pituitary gland (¼ grain [0.016 Gm.] daily), sodium iodide (2 drops daily of saturated solution), biweekly injections of an anterior lobe pituitary preparation, and thyroid extract (¼ grain daily), the doses being increased as the child grows. After persistent treatment, he reports definite improvement in the mental state of the patient and the disappearance of some of the physical stigmas of mongolism. As the bridge of the nose grows higher, the slant of the eyes is reduced and the skull becomes definitely less square. In this paper Timme does not give statistics as to the number of successes and failures.

From the results of this treatment as well as from diagnostic clinical study, Timme concludes that the insufficiency of the anterior lobe of the pituitary gland is an important, if not a unique factor, in the development of mongolian idiocy. Certainly every victim of this condition is entitled to the benefit of intensive endocrine therapy.

DAVIDSON, Newark, N. J.

FURTHER OBSERVATIONS ON THE EFFECT OF WITHDRAWING LARGE AMOUNTS OF SPINAL FLUID. R. HAHN, Monatschr. f. Psychiat. u. Neurol. **75**:30 (Feb.) 1930.

Repeated lumbar punctures, with the withdrawal of from 20 to 30 cc. of spinal fluid, were found to exert a favorable influence on many patients with

nervous and mental disorders. In a patient showing numerous psychotic attacks of an atypical nature, the symptoms became much less marked or disappeared completely after the first lumbar puncture. As a rule, a recurrence took place in two or three weeks, but a second puncture generally led to complete recovery. This was observed in several attacks, the free intervals lasting from five to twelve months. In one case of migraine and two cases of epilepsy in children, repeated punctures were followed by complete cessation of the attacks as well as a definite amelioration of the mental symptoms; in two other cases of epilepsy, the seizures became less frequent. Similar treatment produced a marked improvement in one patient with symptomatic epilepsy of unknown etiology and in two patients with congenital syphilis in whom the only manifestations were convulsive attacks. The same procedure was employed with good results in feebleminded children exhibiting abnormalities of behavior that could not be explained on the basis of the mental deficiency. The author does not believe that the success of this method of treatment is dependent solely on the relief of increased pressure of the spinal fluid, for in some of his cases the pressure was so low that only a small quantity of fluid could be removed. He ascribes the favorable results to the fact that each lumbar puncture is followed by an increased permeability of the blood-cerebrospinal fluid barrier, as shown by Walter's bromide test.

ROTHSCHILD, Foxborough, Mass.

ON THE DETERMINATION OF INTRACRANIAL TENSION BY THE OPHTHALMODYNAMOMETRIC METHOD OF BAILLIART. KNUD WINTHER, Acta psychiat. et neurol. **5**:403, 1930.

The author considers that the ophthalmodynamometric method of Bailliart for determining intracranial tension is as valuable as and less dangerous than manometric studies of the spinal fluid. The technic of the method is as follows: a special manometer is applied to the eye, and the intra-ocular pressure is gradually increased. Normally, such an increase of pressure stops the pulsations in the central artery of the retina. If intracranial pressure is increased, the pulsations become more forcible in order to overcome the increased pressure on the vessel; consequently, it will require more pressure on the eyeball to cause the pulsations to disappear. The method is not reliable if there is hypertension or arteriosclerosis of the artery.

The author examined, in all, 135 patients suffering from neurosis, cerebral trauma (with or without fracture of the skull), encephalitis, meningitis, multiple sclerosis, acute encephalomyelitis, retrobulbar neuritis, cerebrospinal syphilis, frontal sinusitis, cerebral meningitis, labyrinthitis, meningeal hemorrhage pachymeningitis hemorrhagica and tumor of the brain. (In 7 of the 15 cases of tumor of the brain showing increased pressure, this increase was found before any choking of the disk appeared and in 1 case the difference in the pressure in the two eyes aided in localizing the side on which the tumor was located.) In 58 cases the pressure of the cerebrospinal fluid was also determined. Of these, the results of 2 examinations coincided in 42; in 11, Bailliart's test gave an increase in intracranial pressure while the pressure of the cerebrospinal fluid was normal; in 5, the opposite was true.

PEARSON, Philadelphia.

PSYCHOANALYSIS AND PSYCHIATRY. ERNEST JONES, Ment. Hyg. **14**:384 (April) 1930.

Deploring the practical isolation of psychology, psychiatry and neurology, Jones insists that until these sciences can achieve a marked degree of harmonious cooperation there will be no progress in mental hygiene. The connecting link among the three is supplied by a study of the neuroses. Recently there has been tremendous professional and popular interest in the field of the study of the mind, due, Jones believes, to the awakening of the conscience of society appalled by the presence of the great increase in delinquency and mental disease.

That leadership in this movement should have been taken by medical men rather than psychologists is, he thinks, a significant and strange fact. It is due, he suggests, to the realization that the mechanisms of the diseased mind are simpler than those of the healthy mind. In accepting the contribution of psychoanalysis to this, America has been more open minded than profound, and the understanding of the freudian hypothesis in America is more widespread and likewise more superficial than the concept of psychoanalysis held in Europe. Psychoanalysis is compared in its relationship to psychiatry with histology in its position in anatomy. Not only does it give the finer details, but it also explains embryologic development. Thus, it was psychoanalysis that first showed that the neurotic symptoms were efforts at healing, not processes of disease. Psychoanalysis has also given a better understanding of the organic psychoses; Jones believes that the ego is weakened by the organic toxin and failing to adjust, as explained by psychoanalytic mechanisms, it breaks down into the psychosis. The author's conclusion is that between social psychology on the one hand and mental medicine on the other, psychoanalysis will be the important connecting link.

DAVIDSON, Newark, N. J.

THE INFLUENCE OF ULTRA-VIOLET RAYS ON THE CEREBROSPINAL FLUID. E. MEUMANN and O. RIEBELING, Arch. f. Psychiat. **90**:302, 1930.

The authors report a series of experiments in which cerebrospinal fluid and diluted blood serum were subjected to the influence of ultraviolet rays. The construction of a special apparatus for this purpose is described briefly. The cerebrospinal fluid is placed in a porcelain container, and the ultraviolet rays coming from a lamp at a distance of 32 cm. (in some of the experiments, 16 cm.) are directed on this container through the intervening medium of a running stream of water. The effects of the rays on the Wassermann reaction and other immunologic tests, as well as the albumins and total nitrogen in these fluids, were studied. The observations are summarized as follows: (1) The ultraviolet rays cause a reduction in the strength of the bodies that are responsible for the Wassermann reaction in the cerebrospinal fluid. In most cases the Wassermann reaction becomes negative. The length of time necessary for this change differed with the fluids of different patients. (2) The complement and normal amboceptor of the serum and the latter in the cerebrospinal fluid also seem to suffer a decrease in strength and quantity when subjected to ultraviolet rays. (3) The albumins of the cerebrospinal fluid and of the diluted serum are decreased in quantity under the influence of these rays. Outside of the absolute decrease, there is a further relative decrease of the albumin and an increase of the globulin. (4) These changes are accompanied by a change in the colloidal tests in the cerebrospinal fluid. (5) There is a change of color (yellowish brown discoloration) and odor of the cerebrospinal fluid. (6) There seems to be no correlation between the destruction of the Wassermann bodies and that of the albumins in the cerebrospinal fluid.

MALAMUD, Iowa City.

EFFECT OF PILOCARPINE IN CASE OF SYMPATHETICOTONIA IN CHILDHOOD. E. M. LANDIS and J. C. GITTINGS, Am. J. Dis. Child. **39**:1022 (May) 1930.

Landis and Gittings present the case of a girl, aged 10, with attacks of abdominal pain, constipation and leukocytosis. Appendectomy failed to relieve these symptoms. Further studies showed that each attack was accompanied by sweating, dilated pupils, increased blood pressure, glycosuria and tachycardia. Pharmacodynamic tests were performed, and it was found that intravenous injections of atropine, starting with $\frac{1}{600}$ grain (0.2 mg.) and increasing to $\frac{1}{150}$ grain (0.4 mg.) raised the pulse rate from 96 to 152; intramuscular injections of 5 minims (0.3 cc.) of a 1:1,000 solution of epinephrine caused a marked reaction, including tremors, thirst and a rise in blood pressure from 109 (systolic) to 150.

On the basis of these symptoms and tests, a diagnosis of sympatheticotonia was made. Physostigmine salicylate 1/60 grain (1 mg.) injected intramuscularly at the beginning of an attack would abort the episode. Pilocarpine hydrochloride administered by mouth in doses of 1/24 grain (2.7 mg.) was found efficient in relieving pain and shortening the attacks. Thyroid extract and atropine, on the other hand, made the attacks worse. The therapy finally adopted was the oral administration of pilocarpine 1/24 or 1/16 grain (2.7 or 4 mg.) daily. As long as this medication was continued the child was free from attacks, gained weight and attended school regularly. Discontinuation of the drug resulted in discomfort and uneasiness, but not in return of the pain. Sherwood believes that many of the so-called "gastric neuroses" would respond to this sort of therapy. Their case, the authors conclude, is one of true sympatheticotonia.

DAVIDSON, Newark, N. J.

SYRINGOMYELIA OR MYELODYSPLASIA. HENRY A. RILEY, J. Nerv. & Ment. Dis. **72**:1 (July) 1930.

A comprehensive review of the literature on syringomyelia or myelodysplasia suggests that in both these conditions there is an implication of the closure process of the neural tube, the former exhibiting the inclusion of embryonal spongioblasts retaining their undifferentiated condition until the moment of incitement to abnormal activity, the latter representing a more definitely constitutional hereditary predisposition and being associated with other evidence of organized dysgenesis. In most cases the clinical picture of syringomyelia is insidious in development and based on the destruction of the ventral horn cells in the gray matter adjacent to the expanding intramedullary neoplasm. Later, the decussating fibers of the spinal thalamic tracts conveying sensations of pain and temperature become involved in producing the syndrome typical of syringomyelia in the dermatomes affected. The clinical picture of myelodysplasia presents a more static condition in which the striking disturbance is that of trophic and vasomotor control. Although widespread evidence of dysgenesis may occur in both conditions, yet that in myelodysplasia seems more organized and definite. Familial and hereditary characteristics are recognizable in both syringomyelia and myelodysplasia, but are more systematized in the latter.

A family in which seven members showed varying degrees of trophic and dysplasic symptoms in the lower extremities, more marked in the older members of the family, was studied in considerable detail. There was less systematic developmental disturbance than in other families reported by Bremmer, Fuchs and others; the family reported by the author did not show the progressive symptomatology of syringomyelia, but seemed to indicate an inherited lumbosacral disturbance.

HART, Greenwich, Conn.

REACTION TO ANTIMENINGOCOCCUS SERUM. A. DURYEA, J. A. M. A. **95**:1582 (Nov. 22) 1930.

During several quarantine periods for epidemic cerebrospinal meningitis at Maliola Island, Honolulu, T. H., Arthur Duryea, Honolulu, T. H., says that early diagnosis and prompt treatment proved the most effective agent in obtaining a low mortality rate (14 per cent). Quarantine conditions were such that it was possible to isolate and treat patients in the very earliest hours of the disease. It was decided that any patient with the following signs and symptoms should have a diagnostic spinal tap and prophylactic administration of antimeningococcus serum: (1) headache; (2) fever (over 38 C., or 100.4 F.) with no obvious cause; (3) either a positive Oppenheim reflex or Gordon reflex. In many of the cases tapping was done so early in the disease that clear spinal fluid under increased pressure was found on the initial tap, but with no abnormality of chemistry or cell count. On subsequent examinations a high cell count, absence of sugar, positive globulin and characteristic organisms were found. In some cases several days

elapsed before organisms were found either by culture or by direct smear. It seemed necessary, therefore, to ascertain the response of normal individuals to the intraspinal administration of antimeningococcus serum. Two normal healthy men who had not been exposed to epidemic cerebrospinal meningitis were selected as controls. Twenty cubic centimeters of spinal fluid was withdrawn by cisternal puncture and replaced by 20 cc. of a concentrated serum preparation. Subsequently six cisternal and lumbar punctures were done, and fluid removed for examination only. In Duryea's cases of epidemic cerebrospinal meningitis the response of the spinal fluid differs only in the continued presence of sugar in normal, or greater than normal, amounts, and in the absence of bacteria.

EDITOR'S ABSTRACT.

NEUROPATHIES OF THE BONES AND JOINTS. A. R. SHANDS, JR., Arch. Surg. **20**:614 (April) 1930.

Deploring the absence of an adequate classification of the neuroarthropathies, Shands suggests that these conditions may be divided into four groups according to the primary conditions: the peripheral nerve class, including those seen in injuries and neuritis; the lesion of the cord group, including congenital malformations, injury to the cord and acute and chronic infections; the cerebral group, as, for instance, the arthropathies associated with dementia paralytica or hemiplegia, and a group for certain common conditions, such as tabes dorsalis and syringomyelia, which are too common for inclusion in the cord group.

The arthropathy of peripheral nerve conditions tends to take the form of an atrophic arthritis. This is true also of the bone and joint complications of lesions of the cord. Shands quotes Turney in expressing an opinion that the arthropathy of central nervous system origin is due to irritation of the sensory tracts leaving the joints. In the cerebral group, the frequent disturbance of the shoulder joint seen in hemiplegia is cited. In regard to syringomyelia and locomotor ataxia, the Charcot joint is the common arthropathy. This is a painless swelling with cartilaginous changes giving rise to luxations. In tabes the lower extremities are commonly involved and in syringomyelia, the upper. The paper concludes with the report of a case of hypertrophic arthropathy in an ankle which necessitated amputation. The posterior tibial nerve in cross-section showed an enormous increase in interfascicular connective tissue. Shands supposes that the irritation of this nerve, as evidenced by the fibrosis, was responsible for the trophic changes causing the arthropathy.

DAVIDSON, Newark, N. J.

THE ACTION OF ADRENALINE AND CERTAIN DRUGS ON THE ISOLATED HOLOTHURIAN CLOACA. LELAND C. WYMAN and BRENTON R. LUTZ, J. Exper. Zool. **57**:441 (Nov. 5) 1930.

The effects of epinephrine and of certain drugs on the isolated cloaca of *Cucumaria frondosa* and *Stichopus moebii* were determined. The effective dose of epinephrine chloride produced a progressive decrease in tone, amplitude and rate, with a final cessation of beat. Epinephrine caused a marked acceleration of the beat of the intestinal blood vessel of *Stichopus*. Physostigmine, nicotine and histamine produced a progressive increase in tone and a decrease in amplitude and rate. Physostigmine and nicotine sometimes initiated beating in a quiescent preparation. In the case of histamine, there was a tendency for a relatively early recovery from its effects. Curare, strychnine and atropine produced a cessation of beat, usually preceded by a decrease in amplitude and rate. The tone was unaffected or slightly decreased by these drugs. Pilocarpine was generally ineffective. Epinephrine produced the typical inhibitory effect after doses of curare or histamine, but was ineffective following the administration of physostigmine or nicotine. Following the use of cocaine, ergotoxine or an ineffective dose of atropine, there was evidence of a reversal of the inhibitory effect of epinephrine. Cocaine and ergotoxine produced no visible effect when used alone.

It is pointed out that epinephrine has both inhibitory and excitatory effects on invertebrate tissues. The apparent similarity of the action of the drugs used on the holothurian cloaca to the action of the same drugs on mammalian intestine is discussed. It is concluded, however, in view of the absence of adequate morphological data, and the uncertainty of reasoning from the antagonistic action of drugs, that speculation concerning the neuromuscular organization in holothurians and its physiological relation to that of higher forms is futile.

WYMAN, Boston.

A NEW METHOD OF INVESTIGATING THE FUNCTION OF THE CENTRAL NERVOUS SYSTEM. G. MARINESCO, O. SAGER and A. KREINDLER, Arch. f. Psychiat. **90**:517, 1930.

The authors report the results of a study of chronaxie in cases of disease of the central nervous system. They summarize them as follows: (1) The chronaxie affords an opportunity of studying the rate and intensity of the different physicochemical processes of stimulated tissues. A pathologic value for chronaxie shows that there has been a change in these processes in the muscle or the nerve. (2) In tetanus there is a tendency to an equalization of the chronaxies of different muscles. Those that have high values are lowered and vice versa. The authors attribute this to the pronounced affinity of this toxin for the anterior horn cells. (3) In postencephalitic parkinsonism all chronaxies become increased. (4) The rigid muscles of the decerebrated cat have two types of fibers. In the one there is an increase of the chronaxie to three or four times as much as normal, whereas in the other there is a diminution to half the normal value. In a case of decerebrate rigidity in a human being it was found that the chronaxie of muscles which contract in the course of the reflex became shortened, whereas the chronaxie of the antagonists remained unaffected. (5) The passive extension of a muscle in paralytic contracture causes a decrease of its chronaxie, whereas the chronaxie of its antagonists either does not change at all or increases. (6) In tabes there is also a disturbance of the relationship of the chronaxies of the synergists and of the antagonists.

MALAMUD, Iowa City.

THE IMPORTANCE OF DISTURBANCES OF HEPATIC FUNCTION IN ENDOGENOUS PSYCHOSES. F. MEYER, Monatschr. f. Psychiat. u. Neurol. **75**:98 (Feb.) 1930.

In view of the statements of some writers that there is an intimate relation between disorders in the function of the liver and endogenous psychoses, the administration of liver was used by the author in a number of patients with affective and schizophrenic psychoses. This treatment, however, did not meet with success. In order to throw light on the condition of the liver in such diseases, the carbohydrate, fat and protein metabolism was studied in four manic-depressive patients and in an equal number of schizophrenic cases. The protein metabolism was investigated by determining the amino-acid content of the urine after giving glycocoll intravenously. Information in regard to the fat metabolism was obtained by estimating the cholesterol content of the blood at definite intervals following the oral administration of that substance. The blood sugar curve was used as an index of carbohydrate metabolism. The author found that two schizophrenic patients showed cholesterol and sugar curves indicative of liver hyperfunction and hypofunction, respectively. The blood sugar curves were normal in all of the manic-depressive patients; the cholesterol values, however, exhibited changes suggestive of insufficiency of the liver in one patient and hyperfunction in another. No disturbances of protein metabolism were observed in either the manic-depressive or schizophrenic patients. The author does not believe that his abnormal observations can be adequately explained on the basis of some disease of the liver which is related to the psychosis. He is more inclined to regard them as expressions of constitutionally conditioned individual reactions of the organism.

ROTHSCHILD, Foxborough, Mass.

THE EFFECT ON THE SKIN OF EMOTIONAL AND NERVOUS STATES. JOHN H. STOKES, Arch. Dermat. & Syph. **22**:803 (Nov.) 1930.

The psychic background in certain cases of itching is emphasized by Stokes, who points out that it may be a conversion phenomenon, a sexual symbol or an onanistic gratification. He presents three cases in which sexual stress seems to be a factor. In one case, the patient was a woman whose husband was sexually inadequate and who suffered from premature ejaculations; she would have an itching of the thighs and buttocks to which she would respond by furious scratching. After an interview with the husband, the patient became pregnant and there soon occurred striking improvement in the itching. Stokes also recalls a patient who refused to allow treatment for ringworm, because he admitted frankly that scratching this gave him greater pleasure than sexual intercourse. In Stokes' second case, the patient was a man whose itching occurred only at night. He had a night nurse who used to scold him, and the more severely she reproached him the greater the desire to scratch and the more delightful the pleasure it afforded. Sometimes when the nurse was very disagreeable, he would excoriate the skin, and his emotions would rise to the point of ecstasy. This case exemplified the masoschistic-sadistic complex in which sexual pleasure was received both by giving and by being given pain. In the third case, the patient had the nurse rub him when his skin itched. During this process he would caress her hand, and would strain himself; his penis would become turgid. In this patient, scratching between the scapulae produced an emotion which, Stokes said, had the strength and quality of an orgasm. This same man would be entirely relieved of itching when he had sexual intercourse. The treatment of such patients, Stokes concludes, belongs more to the neuropsychiatrist than to the dermatologist.

DAVIDSON, Newark, N. J.

A FOLLOW-UP STUDY OF HYSTERICAL REACTIONS IN WAR VETERANS. P. JOLLY, Arch. f. Psychiat. **89**:589, 1930.

The author reports a study of 420 cases which he has followed since the World War. In some cases compensation was being paid on the basis of functional disease that had developed during the war. Most of the cases were studied by means of questionnaires. Thirty-three patients had either died or developed organic disease. Of the remaining 387 patients, 94.6 per cent have recovered and are at present able to work; 36 per cent of these have no complaints; the others still show some hysterical manifestations. Although 28 per cent of all patients who have received compensation are still being paid, only 10 per cent are actually entitled to it.

Feeblemindedness seems to play an important part in the persistence of the complaints; 38 per cent of those who are still receiving compensation are definitely intellectually subnormal. A review of 14,708 compensation cases of the Düsseldorf district shows that 1.88 per cent show hysterical reactions, and in the whole German army, 15,300 represents the number of hysterical patients receiving compensation.

As to treatment and management, the author finds that his studies show definitely that a knowledge of the more modern concepts of neurosis is of distinct help to both the patients and the community. He suggests that further studies would be rendered more easy if the physicians who examine the patients would also give evidence in court and be responsible for recording the facts for future reference.

MALAMUD, Iowa City.

FINDING A WAY IN MENTAL HYGIENE. F. E. WILLIAMS, Ment. Hyg. **14**:225 (April) 1930.

Seven hundred thousand persons in this country, now going daily about their work and play, apparently well adjusted, are definitely ticketed for state hospitals within the next ten years. This conclusion is based on statistical evidence, and

presumes no increase in the admission rate to mental hospitals. To find these persons long before they reach the stage of frank madness, and to discover and abort the illness, if possible, is the aim of mental hygiene. The medical director of the National Committee devoted to that end reviews the methodology of prophylactic psychiatry, considering first the problem of delinquency. He emphasizes that the scientific approach is not the sentimental approach, that its aim is the protection of the community and not the coddling of the delinquent; he dwells briefly on the value of psychoanalysis, or rather on the psychoanalytic point of view. He insists on the great importance of child guidance work, recalling White's characterization of childhood as the "golden age of mental hygiene." He calls attention to the necessity of educating parents, commenting on the fact that parenthood is the only profession that can be practiced without training. He concludes with the opinion that further progress in mental hygiene hinges on the development of an adequately trained personnel, and he makes a plea for the better psychiatric and social training of physicians working in this field, and for the thorough social, legal and psychiatric education of all nonmedical workers in this subject.

DAVIDSON, Newark, N. J.

METASTATIC ABSCESSES OF THE BRAIN; A CLINICAL STUDY. HARRY L. PARKER, Am. J. M. Sc. **180**:699 (Nov.) 1930.

In a review of twenty proved cases of metastatic abscess of the brain, attention is called to the individual character of each case. There were three main groups of cases: 1. In three cases, the cerebral abscess was only part of an overwhelming general septic process, with organisms in the blood stream, endocarditis and multiple embolic abscesses and finally death in a short time from the general infection. 2. In fourteen cases, metastatic abscess of the brain was secondary to pulmonary and pleural suppuration. The infrequency of cerebral involvement in diffuse septic conditions, in contrast to the frequency of cerebral involvement in suppurative pulmonary disease, is still a puzzling problem. The author made no attempt to separate cases due to empyema from those due to bronchiectasis or abscess because of the latter's interrelationship. Of the fourteen cases, thirteen were in men and one in a woman; the average duration of the illness from the signs of cerebral disease to the death of the patient was nineteen days; leukocytosis was present in ten of thirteen cases, and in ten in which the fundus had been examined there was no papilledema. In half of the cases the abscess was solitary; in the other half there was more than one abscess. 3. In three cases metastatic abscess of the brain developed secondary to an infection that had subsided. The course of symptoms in this group was slow, three and one-half months, and often suggested a diagnosis of tumor of the brain since the original infection was much in the background.

MICHAELS, Detroit.

A CASE OF PERIODIC PARALYSIS. H. KUTTNER, Monatschr. f. Psychiat. u. Neurol. **74**:237 (Dec.) 1929.

The author reports a case of periodic paralysis which presented some unusual features. There was no familial history of the disease. Most of the attacks occurred during the evening or shortly before midnight. The case showed some resemblance to myasthenia in that the orbicularis oculi gave the myasthenic reaction on electrical stimulation during the attack, although it did not take part in the paralysis. The bulbar muscles were somewhat involved in the process. There was a marked increase in the calcium and lactic acid content of the blood, the former ranging from 20 to 47 mg., and the latter from 36 to 48 mg. per hundred cubic centimeters. The calcium was within normal limits on one occasion only, when the determination was made as the paralysis was clearing up. There were, however, no constant differences between the calcium and lactic acid determinations made during the attacks and the ones obtained in the free intervals. The author

does not attempt to explain the marked variations in the values for calcium. He points out that other writers have reported the most varied anomalies of metabolism in familial periodic paralysis. Taken in conjunction with his observations, he believes that this indicates that the basis of the disorder is to be sought in some disturbance of the vegetative or endocrine metabolic equilibrium. He suggests the possibility that the exact nature of the disturbance may differ from case to case.

ROTHSCHILD, Foxborough, Mass.

SOME NEW METHODS FOR STUDYING BRAINS OF EXCEPTIONAL PEOPLE. C. VON ECONOMO, J. Nerv. & Ment. Dis. **72**:125 (Aug.) 1930.

Efforts to study the relationship between structural peculiarities of a brain and individual characteristics have been hampered by a reluctance to destroy the hemispheres by making serial sections of the cerebrum. Preserving the configuration of the brain by making casts has been unsatisfactory because the paraffin and plaster would destroy the cortex. Von Economo recommends a colloidal-mucilaginous rubbery preparation devised by Poller, which becomes rigid at body temperature and does not injure the gray matter. The material is oily when warm, and it is brushed on the brain and painted into the convolutions and furrows. When it hardens it forms a thin shell which by virtue of its elasticity and flexibility permits the underlying brain to be removed without injury. Wax can be poured into this cast and a veritable model of the brain will be produced, reproducing exactly its configurational peculiarities and its absolute measurements. Von Economo suggests that the waxy substance prepared by Poller, called hominit, be used in making the positive cast. To allow for the enlargement of the brain that almost always follows removal from the cranium, a wax model of the inside of the skull should be made. When these models have been constructed there is no reason for not sectioning the brain and subjecting it to careful microscopic study. By preserving the negative cast many reproductions of the same brain may be made. The universal adoption of some standard and practical method such as this will, von Economo believes, contribute materially to the advancement of knowledge of the physiology of the brain.

DAVIDSON, Newark, N. J.

A HISTOLOGICAL BASIS TO EXPLAIN CONSTANT DIFFERENCES IN ACTION-CURRENT RESPONSE FROM CERTAIN POINTS ON THE RETINA OF THE HORNED TOAD, PHRYNOSOMA CORNUTUM. CLYDE E. KEELER, J. Morphol. & Physiol. **50**:193 (Sept. 5) 1930.

The gross appearance of the eye and histologic observations of the retina of *Phrynosoma cornutum* are described. The visual elements consist entirely of many varieties of cones. Fovea and pecten are well developed. The central diagonal light band visible in the fresh retina corresponds to a zone of low "B" rise response ("negative response" of Chaffee) in contrast with zones above and below. The fact that sometimes no response is given when the exploring electrode rests in the foveal depression is explained as being due to the fact that the electrode taps no ganglionic fibers and that leakage due to liquid would be greatest in the pit of the fovea. The fact that no response is elicited from the pecten is explained as being due to its spongy nature, causing leakage, and because no impulse paths are tapped by the electrode. Relief maps of "B" rise heights for "on" and "off" effects were prepared, and diagrams of cross-sections of the retina as well as corresponding curves showing the density of cone distribution were prepared. Curves of height of the "B" rise were superimposed on the curve of density of cone distribution. In general, height of response is inversely proportional to the density of cone distribution. This is explained on the assumption that all cones may bear similar negative charges. The amount of change in potential due to the average cone is calculated to be of the order of 23 billionths of a volt for the "on" effect and 11 billionths of a volt for the "off" effect.

WYMAN, Boston.

THE VIBRATORY SENSE IN NEURALGIA. M. S. BUSIK, Arch. f. Psychiat. **90:** 34, 1930.

The author reports observations on the vibratory sense in a large number of cases of neuralgias of different types, arthritis, lumbago, rheumatism and paralysis of the facial nerve. He comes to the following conclusions: In all cases of neuritis of peripheral type, acute as well as chronic, there is usually either an absence or obvious diminution of the sense of vibration. In neuralgias of different types (sciatic, brachial or plexus) the sense of vibration is either markedly diminished or absent in about 85 per cent of cases. This disturbance shows itself in the clearness, intensity or duration of the perception. In cases of sciatica the disturbance runs parallel to the other signs such as Lasègue and others. This phenomenon would lead one to assume that neuralgia is not a functional disease, but that it depends on an actual neuritic involvement of the nerve.

Busik found that in cases of pain due to arthritis, lumbago or myalgia, there is no disturbance of the sense of vibration, and consequently the testing of this sense is helpful in differential diagnosis. The loss of vibratory sense persists for a long time. It never comes back in cases of sciatica in which the achilles reflex is absent. In some cases, furthermore, when this reflex has reappeared, the sense of vibration still remains either absent or diminished. The testing of this sense also helps in a differential diagnosis between hysteria and actual neuralgia. In all cases of hysteria in which a functional neuralgia was found, the vibratory sense remained undisturbed.

MALAMUD, Iowa City.

HERPES ZOSTER OPHTHALMICUS LUETICA. I. PARDEE, Arch. Ophth. **3:**748 (June) 1930.

This paper considers only the symptomatic type of herpes ophthalmicus. The epidemic type, which has an entirely different etiology and course, is an entirely different clinical entity. The etiology or histopathology of the usual form of symptomatic herpes zoster ophthalmicus is discussed. A syphilitic relationship is obvious when the disease is associated with other positive syphilitic lesions, such as dementia paralytica, tabes or syphilitic meningitis, but when it stands alone, it is liable to be overlooked. Because of this, the author in considering the various writers who have discussed this possible etiologic factor, the variability of the structures involved and a careful survey of his short series, expresses the belief that an astonishing number of cases with a syphilitic etiology could be revealed. With the willingness, only too common, to ascribe every pathologic state, from glaucoma to constitutional psychopathy, as a result of syphilis, the reviewer feels justified in interposing this discordant note of warning — it is possible that a much higher percentage of cases of herpes zoster ophthalmicus may also be "luetica," but the statement that this incidence is an astonishingly large one cannot be passed unchallenged. A brief recommendation of the treatment to be carried out concludes the article. In this, bismuth is given a place of only secondary importance. Actually it should share equally the importance of any other preparation used.

SPAETH, Philadelphia.

A CONTRIBUTION TO THE STUDY OF OCULAR COMPLICATIONS IN MALARIA. J. BISTIS, Ann. d'ocul. **167:**127 (Feb.) 1930.

Malaria may affect practically all the tissues of the eye and adnexa. In the mildest form there is hyperemia of the conjunctiva and of the eyelid, as in the cases of Manhardt. Occasionally there are photophobia and blepharospasm, which usually last for a few hours each day. Marked lacrimation has been reported (Moursou); herpes of the cornea, parenchymatous keratitis and, more rarely, ulcer of the cornea have been noted. Irritation and inflammation of the iris, the ciliary body and the choroid have all been seen. Glaucoma has been noted and described by Bize. In the stage of anemia, retinal hemorrhages are frequently seen and have been reported by Jones, Peunoff, Wormes and Pesme. The optic nerve

may also be involved, and Uhthoff, in studying 256 cases of optic neuritis occurring during the course of infectious diseases, found that 17 were caused by malaria. Neuralgia of the fifth nerve has been reported by several observers, and Orowsky has reported ciliary neuralgia. Paralysis of the muscles of the eyes has also been reported, and bilateral paralysis of the sixth nerve has been seen. Uhthoff, Manhardt, Lavagna and others, have reported paralysis of accommodation and miosis during severe attacks of malaria. Cataract is a rare complication, but it has been seen by Bagot and Kraisky.

BERENS, New York.

THE EFFECTS OF TEN GENERATIONS OF ALCOHOLIC ANCESTRY UPON LEARNING ABILITY IN THE ALBINO RAT. F. B. HANSON and ZOLA K. COOPER, J. Exper. Zool. **56**:369 (May 5) 1930.

In reports prior to the present one the following conclusions were reached: An acquired toleration for alcohol repeated for ten successive generations of inbred rats does not impress itself on the germ cell; rats rendered blind by the direct action of alcoholic vapors on their eyes do not transmit these eye defects to their offspring; data of sex ratio based on large numbers of animals do not indicate that alcohol disturbs the normal sex ratio for albino rats; birth weight is not markedly affected by alcohol, while the size of litters is larger in test than in control animals; finally, the mean body weight of treated and control animals is practically the same at birth and at 20 days, but the growth curve falls off markedly in every generation soon after that time, as the direct result of the treatment. This growth deficiency is not inherited.

In the present report on the learning ability of albino rats, all of the differences between the test and control animals are, with certain exceptions, insignificant. So little positive evidence among so much negative data may possibly be disregarded. At best, the effect is but slight. This is the last of a long series of failures to modify the germ plasm by external agents.

WYMAN, Boston.

IMMUNITY REACTIONS AGAINST CULTIVATED SPIRONEMA PALLIDUM IN GENERAL PARALYTICS TREATED BY INDUCED MALARIA. W. A. CALDWELL, Brit. J. Exper. Path. **11**:1 (Feb.) 1930.

Concerning himself with the problem of whether or not bodies immune to the spirochetes can develop in human tissue, Caldwell studies the agglutination reactions obtained by mixing bouillon cultures of treponemas with various human blood serums. He finds that some nonsyphilitic serums agglutinate spirochetes in the high concentrations, but in dilutions of from 1 to 80 or greater agglutination occurred only with syphilitic serum. The blood from patients with dementia paralytica who had been treated with malaria showed a greater agglutinin content than did the blood of those who had not been treated with serum.

Caldwell also studied the spirocheticidal action of human blood serum. He observed that healthy serum had no power to destroy spirochetes, and that after infection with syphilis this power did not develop. On the other hand, patients treated with malaria, presented serum which had some degree of spirocheticidal activity. The more recently treated cases had a more potent serum than the older ones.

The agglutination tests used here, Caldwell warned, are of no value in the diagnosis of syphilis.

DAVIDSON, Newark, N. J.

THE VISCERAL AFFERENT PATHWAY IN THE ELASMOBRANCH, SCYLLIUM CANICULA. B. R. LUTZ, Biol. Bull. **59**:217 (Oct.) 1930.

With the elaborate morphologic development of the autonomic nervous system in the higher vertebrates, the efferent innervation of the abdominal viscera has tended toward physiologic differentiation. On the afferent side of visceral innervation there is ample evidence in the higher vertebrates that there are fibers running

from the abdominal viscera to the cord by way of the autonomic system. In the elasmobranch fishes one might expect the vagi to take the larger part in carrying afferent fibers from the abdominal viscera, but the writer found in the literature no reference to the vagus as an afferent pathway from these organs. His experiments on *Scyllium canicula* show that the vagus in the elasmobranch is an afferent pathway from the stomach, spiral valve and mesentery. There are no afferent fibers passing through the first large sympathetic ganglion or from the liver and testis, stimulation of which produces either cardiac or respiratory inhibition. Removal of the sympathetic ganglia or destruction of the spinal cord as high as the first vertebra fails to prevent elicitation of the inhibitory reflexes, provided the visceral branches of the vagi remain intact. Faradic stimulation of the central end of a visceral branch of the vagus at the stomach produces cardiac and respiratory inhibition.

COBB, Boston.

ON VENTRICULOGRAPHY. NILS ANTONI, Acta psychiat. et neurol. **5**:249, 1930.

This is a full discussion of the author's experiences with ventriculography. He prefers this to encephalography because of the uncertainty of the distribution of the air, and the terrible headaches resulting from the latter method. In his experience, using the technic he describes minutely, there is only slight risk from ventriculography. He believes it is too early to be dogmatic concerning the diagnostic value of the results obtainable from ventriculography. Its value in the case of cerebral tumors is due to two factors: 1. In a doubtful case, evidence of lateral displacement of the ventricles may settle the diagnosis. 2. It can be used to determine the side on which a tumor located in the silent areas is situated. There are two main groups of tumors from the standpoint of ventriculography: (1) those giving rise to lateral displacement of the ventricles; (2) those causing a diffuse and symmetrical hydrocephalus. The first is the most important sign of tumor. The direct therapeutic result of Antoni's work with ventriculography has been meager. In three cerebellar cases only have the results of examination been of decisively diagnostic import with therapeutic possibilities. The majority of tumors have been inoperable. In none of the epileptic cases were indications for surgical intervention found.

PEARSON, Philadelphia.

POST PROHIBITION ALCOHOLIC PSYCHOSES IN NEW YORK STATE. WILLIAM C. GARVIN, Am. J. Psychiat. **9**:739 (Jan.) 1930.

Up to 1915, there was a steady decline in the percentage of alcoholic patients admitted for the first time to the New York State hospitals, the percentage falling from 11 in 1909 to 6 in 1915. After the war there was a slow and irregular increase, although the number has not yet reached prewar figures. For the last few years, alcoholic psychoses have constituted about 5 per cent of first admissions, while the prewar incidence was seldom below 9 per cent. There has also been a change in the type of alcoholism. Cases of Korsakoff's syndrome have been less frequent, and auditory hallucinations have been commoner in the acute episodes. In a significant communication, Gregory remarked, and Garvin quotes, that chronic alcoholism has largely disappeared since prohibition, but that acute psychotic attacks are just as frequent. In discussing this paper, Englander, of Newark, suggested that many of the psychoses represented syndromes due to poisoning with aldehydes and other chemical by-products of home brew, and that they were not, scientifically speaking, alcoholic.

DAVIDSON, Philadelphia.

THE TREATMENT OF SPONDYLITIS OF THE ATLAS AND EPISTROPHEUS. O. FOERSTER, J. f. Psychol. u. Neurol. **40**:215 (May) 1930.

Foerster describes a new method of treatment that he employed in two cases of severe spondylitis of the atlas and epistropheus with compression of the cord, which threatened the lives of both patients. The method consists in inserting a

piece of fibula of from 12 to 13 cm. in length, between the spinous process of the seventh cervical vertebra and the occiput. The author thus obtains immobilization of the head against the vertebral column and between the uppermost vertebrae themselves, so that the head does not rest immediately on the upper cervical vertebrae but is carried on the piece of fibula implanted against the seventh cervical vertebra. He employed this method successfully in one case of tuberculosis of the atlas and in one case of comminuted fracture of the transverse processes of the atlas followed by a posttraumatic collapse of the latter and compression of the uppermost cervical segments of the cord.

KESCHNER, New York.

THE EFFECT OF SINGLE MASSIVE DOSES OF LIVER EXTRACT ON PATIENTS WITH PERNICIOUS ANEMIA. MATTHEW C. RIDDLE and CYRUS C. STURGIS, Am. J. M. Sc. **180**:1 (July) 1930.

Four patients with pernicious anemia were studied intensively following the administration of single, massive doses of liver extract (three patients received the equivalent of 3,000 Gm. each and one the equivalent of 1,500 Gm. of liver). After two days, marked clinical improvement occurred and the reticulocyte response compared favorably with predetermined standards. Besides a good response in the red and white blood cells and the hemoglobin, definite "blast crises," in which immature forms are revealed microscopically, were found. All of these responses lasted about ten days. The authors confirm the opinion of Minot that the response to medication with liver depends on the total amount of the active liver principle used during a certain period of time rather than on the amount consumed each day.

MICHAELS, Detroit.

CLINICAL DETERMINATION OF THE ALBUMIN GLOBULIN RATIO IN SPINAL FLUID. W. G. EXTON and A. R. ROSE, J. A. M. A. **96**:36 (Jan. 3) 1931.

A method of determination of the albumin globulin ratio is described which separates the two main protein fractions and is a modification of similar methods developed for blood and urine. In principle, the method separates globulin from albumin in the classic way by half saturation with ammonium sulphate, and then determines the concentration of each fraction by scopometry after precipitating the albumin and globulin separately with phenol. Because the sum of the amounts of albumin and globulin obtained in this way corresponds with the total protein results obtained with the protein reagent and scopometry, which corresponds excellently with Kjeldahl checks, it is easier to obtain the concentration of the albumin fraction by subtracting the globulin from the total protein than by precipitating the albumin separately.

EDITOR'S ABSTRACT.

PHENYLETHYLHYDANTOIN IN THE TREATMENT OF SYDENHAM'S CHOREA. H. H. RAY and J. S. CUNNINGHAM, Am. J. Dis. Child. **39**:1205 (June) 1930.

Although it almost always results in a rash and fever, phenylethylhydantoin, commonly known as nirvanol, is a valuable sedative. Ray and Cunningham used this drug in alternate cases of chorea, employing the usual bromides and salicylate sedatives in the control group. They found that the chorea lasted 115 days in the group not treated with phenylethylhydantoin and only 31 days in the patients receiving this remedy. The dose is from 5 to 10 grains (0.324 to 0.65 Gm.) daily, and is given for 9 days. Fever and a rash usually occur, and reach their maximum at the end of the first week. In no case did any harm result from the exanthem or from the rise in temperature. The authors believe that phenylethylhydantoin is a valuable remedy in chorea and that it almost invariably shortens the duration of the illness.

DAVIDSON, Newark, N. J.

CONTRIBUTION TO THE PROBLEM OF THE DEVELOPMENT OF THE SYMPATHETIC NERVOUS SYSTEM. ERNEST VAN CAMPENHOUT, J. Exper. Zool. **56**:295 (May) 1930.

Embryos of *Rana palustris* and *Rana pipiens* were used for the experiments. The experimental procedure consisted of the removal of different parts of the nervous cord with straight or curved iridectomy scissors. Various stages of development were used: wide-open neural folds, closing folds and closed folds that were not yet fused, or those that had just been fused. Two kinds of operations were performed: the removal of the dorsal half of the nervous system from the medulla caudalward, and the removal of the medulla itself. Subsequent study of the preparations led to the conclusions: the neural crest is the exclusive source of the sympathetic elements; the visceral part of the vagus nerve is derived from the medullary neural crest; the intestinal plexus arises from the branches of the prevertebral sympathetic cords and is not related to the vagus nerve.

WYMAN, Boston.

MYXEDEMA DURING THE ADMINISTRATION OF IODIN IN EXOPHTHALMIC GOITER. W. O. THOMPSON, P. K. THOMPSON, A. G. BRAILEY and A. C. COHEN, Am. J. M. Sc. **179**:733 (June) 1930.

The occurrence of myxedema during the administration of iodine in cases of exophthalmic goiter is rare. Cases are cited in which myxedema was produced by the postoperative administration of iodine. After a subtotal thyroidectomy for exophthalmic goiter, temporary medication of iodine may produce a syndrome ranging from temporary myxedema to temporary low metabolism without accompanying signs and symptoms of myxedema. Some of the theories as to the action of iodine in exophthalmic goiter are discussed. It is concluded that the myxedema that develops is due to an inhibition of the secretion of the normal hormone of the thyroid, and that iodine may cause a reduction in the high basal metabolism of exophthalmic goiter in the same manner.

MICHAELS, Detroit.

UNRECOGNIZED RETINOBLASTOMA AND PSEUDORETINOBLASTOMA. MARTIN COHEN, Arch. Ophth. **4**:368 (Sept.) 1930.

This is a report of an unrecognized case of glioma retinae (retinoblastoma) and of a case of pseudoglioma, both with unusual histories and observations. The microscopic pathology, through the study of sections, is included. Illustrations in colors are also included in the text. In the first case an early diagnosis of metastatic ophthalmia was made and not changed to glioma retinae until a hemorrhage developed in the anterior chamber. In the second case a diagnosis of glioma retinae was made, and the section showed it to be a plastic cyclitis with cyclitic membrané, consecutive retinitis proliferans and retinal detachment.

Enucleation was properly done in each instance, however; in the first case, because of the final diagnosis, and in the second because the patient had a blind, painful, degenerating eye with secondary glaucoma — a condition well treated by the enucleation.

SPAETH, Philadelphia.

THE INCIDENCE OF CONGENITAL SYPHILIS IN AN INSTITUTION FOR THE FEEBLE-MINDED. CHARLES WOODALL, Am. J. Psychiat. **9**:1065 (May) 1930.

In examining more than 1,300 inmates of a colony for the feebleminded, Woodall found clinical and serologic evidence of syphilis in only 7 per cent. Furthermore, many of the patients with congenital syphilis showed a sufficiently defective heredity to account for the feeblemindedness on the familial basis alone. In the course of his serologic studies, the author found that the Hinton glycerol-cholesterol precipitation-agglutination reaction was more sensitive than either the Kahn or the standard Wassermann test. In spite of the low incidence of syphilis in this

institution, Woodall believes that many cases of mental defect are caused by congenital syphilis, and he supports this conviction by citing statistics demonstrating feeblemindedness in 20 per cent of the families of those born with syphilis.

DAVIDSON, Newark, N. J.

JAMAICA GINGER PARALYSIS. R. H. GOODALE and M. B. HUMPHREYS, J. A. M. A. **96**:14 (Jan. 3) 1931.

The autopsies of three patients with jamaica ginger paralysis dying of other causes are presented. A study of the nerves shows an acute inflammation of one segment of the cauda equina in one case, and myelin sheath and axis cylinder degeneration of the radial, sciatic, external popliteal, anterior tibial and posterior tibial nerves in all three cases. The degeneration is found as high as the gluteal fold in the sciatic nerve but not in the anterior roots of the lumbar cord. These observations are consistent with the observations in a follow-up clinic in which it was found that all patients showed marked improvement of wrist and finger motion and little or no improvement of foot motion from five to six months after the onset of paralysis.

EDITOR'S ABSTRACT.

EXPERIMENTAL STUDIES OF THE NERVOUS PHENOMENA OF POISONING WITH VITAMIN D. HANS HOFF, Ztschr. f. d. ges. Neurol. u. Psychiat. **126**:149 (July) 1930.

Hoff found changes in the nervous system in vigantol (vitamin D) poisoning in animals. These changes were degenerative. No inflammatory changes were found. The nerve cells showed evidence of homogeneous appearance and tigrolysis, and the neuroglia showed proliferative changes, particularly the microglia. There was degeneration of the peripheral nerves. Hoff found that removal of the pituitary gland led to the appearance of changes in the vessels and bones in vigantol poisoning, while removal of the thyroid produced cerebral changes more readily. The induction of an Eck fistula led more readily to cerebral symptoms. Vitamin D enters the nervous system by way of the spinal fluid.

ALPERS, Philadelphia.

THE VASCULARITY OF THE CEREBRAL CORTEX IN A SPECIMEN OF APTERYX. E. HORNE CRAIGIE, Anat. Rec. **43**:214 (Aug. 25) 1929.

In a single specimen of the brain of *Apteryx* the vascularity in the forebrain is relatively low and that of the cerebral cortex is lower than parts of the corpus striatum. Measurements in both archipallial and neopallial regions are recorded. The layers of the small laminated area which has been described as neocortex have essentially the same mutual relation in point of vascularity as those of the neocortex in the rat, the zone representing the internal granular layer being richest and the supragranular being richer than the subgranular laminae. Thus the quantitative relations of the capillary supply provide additional evidence in favor of the view that these layers are probably homologous with those of the mammalian neocortex.

COBB, Boston.

ENDOCRINE STUDIES: THE ETIOLOGY OF GLAUCOMA. A. W. ROWE, Arch. Ophth. **3**:403 (April) 1930.

In an investigation of the alleged endocrine factor in the causation of glaucoma, Rowe conducted careful clinical studies on twenty-seven patients suffering from that condition. In only one patient did he find definite indication of an endocrine disturbance—this represented a pituitary disorder. There was questionable endocrinopathy in two others, while the remaining twenty-four patients presented no evidence of any ductless gland dysfunction. Rowe concludes, therefore, that there is no reason for assigning any endocrine etiology to glaucoma.

DAVIDSON, Newark, N. J.

SUDDEN DEATH ASSOCIATED WITH BRAIN CYSTS. L. C. KNOX, J. A. M. A. **95**:1813 (Dec. 13) 1930.

Leila Charlton Knox, New York, reports five cases of brain cyst observed post mortem during the course of 2,000 consecutive autopsies including only 321 complete examinations of the skull. Three of these patients died suddenly, having been active up to a short time before death. The series includes three angiomatous cysts, with an hemangioma of the spleen; one congenital cerebral cyst associated with a cavernous angioma of the leptomeninges, and one gliomatous cyst. Attention is drawn to the fact that such cysts may be present and even be a cause of sudden death in apparently healthy persons.

EDITOR'S ABSTRACT.

ACUTE BENIGN INFECTIOUS MYELITIS. I. J. SANDS, J. A. M. A. **96**:23 (Jan. 3) 1931.

Attention is called by the author of this article to a recoverable type of myelitis. Following infection of the upper respiratory channels there occurs, in young persons, paralysis of the lower extremities with loss of deep tendon reflexes, loss of abdominal reflexes, retention of urine, and subjective as well as objective sensory disorders segmental in distribution. There is slight leukocytosis. The spinal fluid shows an increase in protein and relatively little cellular reaction. Recovery is apparently rapid and complete. A relationship between this disease and epidemic encephalitis is suggested.

EDITOR'S ABSTRACT.

PROGRESSIVE LIPODYSTROPHY APPEARING AT MENOPAUSE. F. P. CURRIER and D. B. DAVIS, Am. J. M. Sc. **179**:750 (June) 1930

A case is reported in a woman, aged 65, because the onset of the disease came with the menopause and because the family history suggested the possibility of a hereditary disturbance of fat metabolism. Numerous theories concerned with the etiology of progressive lipodystrophy are discussed. The similarity in the lack of adipose tissue in the trunk and upper extremities in pituitary cachexia, Lorain-Levi syndrome and progressive lipodystrophy are suggestive of a possible pituitary disturbance. No valuable method of treatment has as yet been found.

MICHAELS, Detroit.

TWO ASPECTS OF AFFECTIVITY. HENRI CODET, Ann. méd. psychol. **38**:429 (May) 1930.

In studying emotional disorders one does not, Codet believes, give proper emphasis to the sympathetic nervous system. Many of the tired, unambitious, indifferent patients whom one dismisses hurriedly as schizoid or neurasthenic are really vagotonic; many of the excitable and moody subjects show enough tachycardia, pupillary dilatation and similar signs to warrant a diagnosis of sympatheticotonia. Therapy directed at the sympathetic nervous system, with these facts in mind, will, Codet suggests, often give gratifying results.

DAVIDSON, Newark, N. J.

A CLINICAL STUDY OF RETINITIS. J. CHAILLOUS and M. GARNIER, Ann. d'ocul. **167**:205 (March) 1930.

Chaillous and Garnier report four cases of typical diabetic retinitis in which visual acuity was markedly affected. At the time the blood sugar was studied, the urine was negative for sugar in all four cases. They stress the importance of examination for sugar in the blood as well as in the urine in hemorrhagic retinitis which has many of the characteristics of diabetic retinitis.

BERENS, New York.

THE EFFECT OF FIXATION ON THE CELLULAR PICTURE OF THE CEREBRAL CORTEX. S. A. SARKISSOW, J. f. Psychol. u. Neurol. **41**:265, 1930.

Variations in the duration of the periods during which the brain remains in the skull after death are followed by marked differences in the cellular structure of the cerebral cortex. These differences correspond fully to those described by various authors in the cell structure of the cortex of domesticated animals as compared to that of wild animals.

KESCHNER, New York.

THE TREATMENT OF PERNICIOUS ANEMIA WITH AN EXTRACT OF FISH LIVER. JOSEPH E. CONNERY, Am. J. M. Sc. **180**:603 (Nov.) 1930.

An aqueous extract of the livers of cod, haddock and other members of the *Gadus cal.* family, from which the oil had been removed, was fed to six patients with addisonian pernicious anemia. The improvement was comparable to that of patients treated with whole mammalian liver or with a liver fraction.

MICHAELS, Detroit.

TREATMENT OF DEMENTIA PARALYTICA WITH HYPERPYREXIA PRODUCED BY DIATHERMY. C. A. NEYMANN and S. L. OSBORNE, J. A. M. A. **96**:7 (Jan. 3) 1931.

In discussing dementia paralytica, the authors describe a method for producing hyperpyrexia in man. Twenty-five patients with dementia paralytica have been treated; 66 per cent went into a clinical remission; 8 per cent were markedly improved. No serious harm resulted to these patients from the treatment, and there were no deaths in this series directly or indirectly ascribable to the treatment. Certain physiologic phenomena associated with hyperpyrexia produced by diathermy are described.

EDITOR'S ABSTRACT.

PROGRESSIVE LIPODYSTROPHY OF THE LOWER EXTREMITIES; REPORT OF A CASE. HUGH SMITH, Am. J. M. Sc. **179**:758 (June) 1930.

This article reports the case of a woman, aged 55, in which there was just the reverse of the usual distribution in cases of lipodystrophy. There was a striking contrast in the slenderness of the hips, thighs and legs to the upper portion of the body which was well covered with subcutaneous fat. The disease began after the menopause.

MICHAELS, Detroit.

VARIATIONS IN THE INTRANEURAL COURSE OF THE CENTRAL VEIN OF THE RETINA. W. E. FRY, Arch. Ophth. **4**:180 (Aug.) 1930.

Serial sections of the optic nerves of thirty-six eyes were studied. From this series it was determined that there are at least two different types of anatomic variation of the intraneural course of the central vein of the retina. Diagrams as well as photomicrographs illustrate these types.

ANOMALIES OF ACCOMMODATION. T. D. ALLEN, Arch. Ophth. **4**:84 (July) 1930.

This article is a study of the accommodation in 5,000 consecutive cases to determine the frequency of anomalies of accommodation. A classification of these arose in which the following features were outstanding: premature presbyopia, insufficiency of accommodation, illy sustained accommodation, inertia of accommodation, inequality of accommodation between the two eyes, and excessive accommodation. Each type is illustrated by the report of a case. It was demonstrated that 2 per cent of all cases in a general ophthalmic practice present these anomalies.

SPAETH, Philadelphia.

OPTIC ATROPHY IN IDIOPATHIC EPILEPSY. A. HALLENSLEBEN, Monatschr. f. Psychiat. **77**:99 (Sept.) 1930.

Three cases of epilepsy were studied in which, as a result of optic atrophy, blindness occurred. In these cases the epilepsy was not symptomatic but "idiopathic." In the first case this was corroborated by an autopsy. Degenerative changes leading to atrophy of the optic nerves and the subsequent blindness were found and were regarded as an unusual by-product of a particular localization of the "epileptic brain process." HART, Greenwich, Conn.

FAMILIAL AMYOTROPHIC LATERAL SCLEROSIS WITH MARKED DIMINUTION IN THE SIZE OF THE CORPUS CALLOSUM. G. KREYENBERG, Ztschr. f. d. ges. Neurol. u. Psychiat. **123**:400, 1930.

Kreyenberg reports the cases of three members of one family with amyotrophic lateral sclerosis. All three became ill in the fourteenth year. Two of the cases were studied pathologically. Besides the well known changes of amyotrophic lateral sclerosis, there was a marked decrease in size of the corpus callosum with loss of cells in the area centralis and area limbica. ALPERS, Philadelphia.

A TUMOR OF THE PINEAL ORGAN WITH CARTILAGE FORMATION IN THE MACKEREL, SCOMBER SCOMBRUS. H. H. CHARLTON, Anat. Rec. **43**:275 (Aug. 25) 1929.

The case reported is a chondro-epithelioma involving the pineal organ and the dorsal sac. It has destroyed the pineal organ, the rudiment of the paraphysis and the habenular commissure, but has otherwise caused little if any injury to the brain. A possible explanation may be suggested when the relation of the epiphysis to the neuropore is recalled. COBB, Boston.

THE DIAGNOSTIC VALUE OF THE SUGAR TOLERANCE TEST CURVE IN ENDOCRINOPATHIES. B. Y. GLASSBERG, Arch. Int. Med. **46**:984 (Dec.) 1930.

Finding no constancy in curves for sugar tolerance repeated within a few days in the same patients and unable to find any curve commonly associated with any individual endocrinopathy, Glassberg concludes that the test for sugar tolerance is without value in the diagnosis of endocrine disorders.

DAVIDSON, Newark, N. J.

A CASE OF PARALYSIS OF ASSOCIATED MOVEMENT DOWNWARD. ONFRAY, Ann. d'ocul. **167**:133 (Feb.) 1930.

A case of paralysis of associated movement downward is reported by Onfray in a man aged 54. The condition developed suddenly, with the appearance of a right hemiplegia. All of the movements of the eye and accommodation and convergence were unaffected. BERENS, New York.

Society Transactions

BOSTON SOCIETY OF PSYCHIATRY AND NEUROLOGY

Three Hundred and Eighty-Eighth Regular Meeting, Nov. 20, 1930

E. W. Taylor, M.D., *President, in the Chair*

Dystonia Musculorum Deformans in Siblings. Dr. J. Kasanin and Dr. S. C. Allen.

The patients, sisters, aged 13 and 9, were born in Boston of Russian Jewish parentage. The family history was without significance; there was no consanguinity. Both parents are in good health; the patients are the youngest children in a family of seven; the siblings are well and show no evidence of neurologic involvements. Birth and development in both patients were normal.

The older girl began to show symptoms at the age of 4½, when the parents noticed that she was clumsy, slow and could not run about as well as other children. A year later, contractions and spasms of the various groups of muscles in the upper and lower extremities were noticed. Speech became involved at the age of 9. The intellectual development remained normal. A neurologic examination gave essentially negative results. There were constant spasms of various groups of muscles with contractions of the extremities. There was a contracture of the right lower extremity.

In the younger sister, the symptoms began to develop at the age of 6, with kinetic phenomena in the right leg. Since then, there has been a rapid progression of symptoms with numerous residual contractions. At the present time, the patient shows constant alternations between hypertonus and hypotonus in the flexor groups of muscles in all extremities. Neurologic examination gives otherwise negative results. The intellectual development is normal.

There is no evidence of an encephalitic etiology in these cases. The dystonia is probably a familial degenerative condition.

DISCUSSION

Dr. Stanley Cobb: If there is no history of influenza or injury, I suppose that one must consider this an abiotrophy or possibly a poisoning by lead or some other material reaching both sisters. There is an unsteadiness of ocular movements rather than a true rhythmical nystagmus. In the older patient, the movements are distinctly athetoid and not choreic; in the younger, there are some myoclonic movements, suggesting a degeneration below the red nucleus as well as in the striatum.

Dr. H. R. Viets: In two patients described by Dr. Taylor (Dystonia Lenticularis [Dystonia Musculorum Deformans], Arch. Neurol. & Psychiat. **4**:417 [Oct.] 1920), the signs were not equal on the two sides of the body. One patient had marked torsion spasm in walking and always turned in the same direction. In Dr. Kasanin's patients, the involvement seems approximately equal on the two sides, and there is no torsion spasm.

Dr. E. W. Taylor: This case represents one of a large group of disorders presumably due to lesions of the basal ganglia and adjoining structures. The nomenclature is confusing and rendered more so by the fact that clinical entities are difficult to determine, as they are in many other structural changes in the nervous system. The symptomatology of various conditions described under specific names run into each other in such a way that conditions deserving the dignity of individual diseases are most difficult to establish. Many terms have

been used to describe the symptom-complex exemplified by Dr. Kasanin's patient, among them, torticollis, athetosis universalis, torsion spasm, myasthenia, dysbasia lordotica progressiva, and others of like character. On the whole, the term dystonia lenticularis introduced by Thomolla is to be preferred, since it describes adequately the muscular condition and suggests the anatomic location without the introduction of extraneous factors. Until knowledge becomes more definite, it is desirable to use general terms rather than superficially descriptive ones.

DR. J. KASANIN: The father of the patients is a tinsmith, but we have found no evidence of lead poisoning in any member of the family. The mother used various contraceptive methods, and it is conceivable that this condition is a result of an injury to the germ plasm. Stramonium has been tried without benefit. Dr. Foerster suggested cutting the anterior roots for relief from the symptoms.

DR. M. R. KAUFMAN: I have seen four or five cases of this condition at the Montefiore Hospital, New York, in which disturbances of the gastro-intestinal tract and other symptoms of disorder of the vegetative nervous system appeared. Roentgenograms in some cases showed remarkable changes in the stomach and intestines, a sort of dystonia of the smooth musculature. In these cases a definite encephalitic etiology was elicited. Was there any vomiting, diarrhea or evidence of involvement of the vegetative nervous system in Dr. Kasanin's patients?

DR. J. KASANIN: There was no evidence of involvement of the vegetative nervous system, and only an occasional mild gastric upset in the younger patient.

THE RECENT TYPE OF POLYNEURITIS AND ITS PATHOLOGIC EFFECTS. DR. B. T. BURLEY.

Until recently, it seemed that toxic or multiple neuritis had become comparatively rare. Early in 1930, however, an epidemic of polyneuritis presenting a new symptom-complex appeared in various parts of the country. For a long time the toxic agent was unknown, but recently, largely through the efforts of Dr. Smith, chief pharmacologist, United States Public Health Service, it has been established as tri-orthocresyl phosphate, a substitute used in making an inferior Jamaica ginger.

The first cases in Worcester appeared early in April, and 60 patients were admitted to the Worcester City Hospital alone, there being probably 100 cases in the locality. The paralysis was always bilateral, affecting the anterior tibial muscle group in both legs without prodromal symptoms except temporary paresthesia of the legs. In all severe cases, paralysis of the peripheral nerves of the upper extremities followed in about a week. The paralysis was purely motor, the affected muscles showing the reaction of degeneration by electrical tests. Later, as atrophy of the muscles became marked in the severe cases, there was a diminution of reaction even to the galvanic current.

The reflex changes are characteristic of the disease: the achilles reflex is lost, but that in the knee is practically always present. Vasomotor changes in the extremities are marked by sweating in the early stages and later by cyanosis. The cranial nerves are intact, as are the important organs of the body. The spinal fluid shows no pathologic process. I consider this clinical entity sufficiently cleancut to make a differential diagnosis from other forms of polyneuritis such as those due to lead, alcohol, arsenic and other chemical and infectious agents.

A follow-up of these cases, six months after the onset, showed improvement in the use of the hands in every case, with little improvement in the toe-drop, though locomotion showed some improvement. The treatment consisted of the maintenance of a favorable position for the limbs in the early stages, and massage and training of the muscles in the later stages.

AUTOPSY OBSERVATIONS IN JAMAICA GINGER POLYNEURITIS. DR. RAYMOND H. GOODALE, Worcester, Mass.

During the spring, 1930, when Jamaica ginger polyneuritis occurred in many cities throughout the country, sixty-two patients were admitted to the Worcester City Hospital. Three died in the hospital, and autopsies were done. The three

deaths were precipitated by factors other than the poisoning of the peripheral nerves from the Jamaica ginger which the patients drank. Studies were made of the spinal cord and the radial, anterior tibial, sciatic, external popliteal and posterior tibial nerves.

In the spinal cord, no degeneration of the anterior horn cells was found by staining with hematoxylin and eosin. The peripheral nerves showed degeneration of the myelin sheaths by the Spielmeyer technic. This degeneration was much more extensive in sections of the anterior tibial and external popliteal than in the radial nerves. The Bielschowsky stain showed either an absence or a fusiform enlargement of the axis cylinders in the areas of degeneration of the myelin sheaths. The sudan III stain for fat showed only an occasional droplet of neutral fat in those areas.

A follow-up clinic, held from five to six months after the onset of the paralysis, showed improvement of the extensor function of the hand in all of twenty-two patients who returned. Little or no improvement was noted in the extensor function of the feet. The more extensive injury to the external popliteal and anterior tibial nerves found at autopsy bears out these functional results.

DISCUSSION

DR. CHARLES MCDONALD: A similar epidemic was seen in Providence before that appearing in Worcester. I saw, I think, 140 patients, over two thirds of whom were at the Rhode Island Hospital clinic. The clinical picture was uniform and quite like the clinical picture that Dr. Burley described. As Dr. Burley emphasized, the toxic factor had a selective action on the motor side of the lower and upper extremities. The absence of sensory involvement was characteristic. To date not a single patient has recovered. A good many are improving, and the improvement of the hands is greater than that of the feet. In our series there has been only one death, from a cerebral hemorrhage, but no examination was made of the brain or cord.

DR. S. COBB: In one case which came to autopsy at the Boston City Hospital, there was an acute degeneration of the anterior horn cells. This appeared in the frozen sections, prepared by Dr. Raymond Morrison, as large droplets of fat, and we therefore think that the prognosis in these cases is not good. I thought that there might be merely a degeneration of the axon; if that were the case, one might have to wait almost a year for regeneration of the toe-drops, for it is obvious that the long axons supplying the legs regenerate more slowly than those in the arms.

DR. E. W. TAYLOR: It seemed to me that in the photographs shown there was considerable irregularity in the axons, as well as a lesion in the myelin.

DR. R. H. GOODALE: It is possible that the necessity for the constant use of the hands tends to keep them in better condition than the legs.

DR. B. T. BURLEY: In a personal communication, Dr. Smith of the United States Public Health Service told me that he has found the substance at fault to be tricresyl phosphate. He used various fractions obtained by distillation, and produced typical paralysis in monkeys and calves.

VACCINIAL ENCEPHALITIS. DR. HENRY R. VIETS and DR. SHIELDS WARREN.

The first case of vaccinial encephalitis was described in 1912 by Turnbull and McIntosh, although it was not reported until 1926. Since then, many cases have been described, especially in Continental and in English literature. The first fatality observed in America occurred in 1924; four fatal cases have been reported in the last few years and a number of patients have recovered. Two more cases are added to the American literature in this preliminary report, one with a pathologic examination.

A boy, aged 6, was vaccinated on May 27, 1930, at the same time as a number of other children, including his younger sister. The child was in good health until the eleventh day, when he became drowsy and complained of headache. On

the twelfth day he was stuporous. He entered the hospital on the fourteenth day, and on examination it was noted that there were bilateral ptosis, tonic contractions of the extremities, stiffness of the neck and a bilateral Kernig sign. The pupils reacted readily to light, and the reflexes were not exaggerated. A diagnosis of acute tetanus was made, and tetanus antitoxin given. The child died on the same day.

The sister of the patient, aged 8, was also vaccinated on May 27. On the eleventh day after vaccination, she too became drowsy and complained of headache. The next day she was semistuporous, the pupils were dilated, and there was some rigidity of the muscles of the neck, with trismus of the jaw. The extremities showed slight rigidity, but the reflexes were normal, and there was no clonus or Babinski sign. As in the case of her brother, a provisional diagnosis of tetanus was made, and tetanus antitoxin was administered both intravenously and intraspinally. The patient made a gradual recovery, and in about a week seemed nearly normal. Later, it was noted that she had paralysis of the left foot, which persisted four months later. The paralysis was flaccid and involved both the flexor and extensor muscles of the ankle.

The pathologic changes in the first case were reported by Dr. Warren. There was well marked evidence of encephalitis, especially in the midbrain, which showed moderate congestion with perivascular edema. Polymorphonuclear leukocytes and occasional mononuclear leukocytes were present, and the cells infiltrated for a short distance into the surrounding tissue of the brain. There was some necrosis of the vessels and demyelinization of many adjacent fibers. The polymorphonuclear and mononuclear reaction was extremely marked about certain vessels. Examination of one or two portions of the spinal cord (all that was available) gave negative results.

DISCUSSION

Dr. J. B. Ayer: What does Dr. Warren believe to be the etiology of this condition?

Dr. Charles McDonald: In a case in which we made this diagnosis at the Neurological Clinic at the Rhode Island Hospital, there was double paralysis of the sixth nerve. The paralysis was of sudden onset and gradually lessened so that at the time of discharge, the right eye was normal in position and in motion; the left eye improved greatly, but still showed an internal squint.

Dr. Raymond Morrison: I was interested in the way Dr. Warren classified the cells in the perivascular infiltration. I wonder whether the case is typical of encephalitis post vaccinationem. At one time or another I have seen about fifteen cases of this disease, as well as three cases of encephalitis following measles, which is also characterized by perivascular demyelinization, and invariably the infiltrating cells were microglia.

Dr. T. J. Putnam: Must we assume that this is a virus disease at all? Inoculation experiments of spinal fluid and fresh brain material into many animals, including monkeys, have been performed in Holland and England with entirely negative results, although under favorable circumstances and in the hands of expert investigators. Clearkin produced the lesions in monkeys by cutaneous vaccination, but did not transmit it from brain to brain. About a year ago, I presented a dog before this society in which similar lesions developed following the intraperitoneal inoculation of tetanus toxin. More recently, similar lesions have been produced by certain types of aseptic emboli.

Dr. S. Warren: The exact etiology of this disease is not known. Perhaps the virus hypothesis is on the whole the most tenable. The damage is rather too sharply localized to be due to a toxin in the circulation. We could find no thrombosis or vascular damage in this case.

Dr. H. R. Viets: The spinal fluid pressure was slightly increased, just over 200 mm. of water.

Book Reviews

DIE SEELISCHEN HEILMETHODEN DES ARZTES. EINE LEHRE VOM NEUROTISCHEN MENSCHEN. By MAX LEVY-SUHL. Price, 15 marks. Pp. 280. Stuttgart: Ferdinand Enke, 1930.

Among the flood of presentations of psychotherapy, the present book stands out as the product of a psychotherapeutist who has gone through nonfreudian hypnosis methods to a final adoption of psychoanalysis, largely owing to the appeal of the later freudian metapsychologic writings and the interest in the pathology of conscience. Under the peculiar incubus of the German segregation of natural and mental sciences, the author evidently needed the growing appeal to valuations, processes and the psychopathology of the conscience functions, to add to suggestions and persuasions the analytic process. The proof of the "essential unity of psychotherapy" seems to be given by the intrinsic unity and specificity of "neurotic illness and its psychic cure." He sees an analogy to the dictum of Kant concerning religion, "there is only one true religion; but there can be many kinds of faith." We cannot help seeing in the whole "more than naturalistic" tendency a trait that characterizes much of the pertinent German literature, something foreign to the American trend, unless we accept the frequent lack of critical concern and fear of any philosophic discrimination as the American equivalent, a negative something in the place of a "too much."

The material is presented in 50 chapters, relatively few being more than a few pages long, and is therefore in great contrast to the too solid and nonarticulated presentation of many kindred books. The 280 pages are preceded by no less than 11 pages of a readily grasped and well distributed table of contents with the headings of the discussions and concise references to the 72 brief illustrative cases used. The advantage of this procedure lies in the prevalence of relatively simple, concrete topics, instead of the excessive systematization of generalities.

From a teleologic point of view, the author defines "the neurosis" as a purposeful construction of mental and somatic symptoms derived from the natural impulse of the self-preservation of the mental ego. It has to keep out of the consciousness the inner admonition of the conscience concerning unobserved and unfulfilled demands of the moral personality of man; at the same time the suffering, as well as the emphasis on it, serves to obtain the comforts from the environment and the physician and to mitigate the sense of guilt through the painfulness of the symptom as a self-punishment.

The neurosis is a struggle within the conscience, "a dramatization of self-accusation and self-defense arising from the self-responsibility of the moral autonomy of man, which the neurotic knows and acknowledges in his more than empiric intelligible essence, but denies in his empiric worldly personality."

The wide range of facts, points of view and detailed description of methods makes the book a rather unique presentation, a guide for the simplest as well as the more complex hypnotic and analytic methods with utilization of unorthodox as well as orthodox material derived from wide reading and a large fund of practical experience. With all this recognition one cannot help feeling somewhat uncertain as to the soundness of much of this attitude toward the neuroses and the multitude of approaches, and the "unity" of the psychopathology and psychotherapy and the partly learned and partly uplift-charged ventilations of physicians and patients. We hear the phrase, "the century of the child"; it is also the century of the "talking cure." Or are these only the "naturphilosophie" decades of the twentieth century, a kind of repetition of the same decades of the nineteenth century?

FRÜHSYMPTOME GEISTIGER ERKRANKUNGEN. By DR. ERNST WITTERMANN. Price, 1 mark. Pp. 32. Leipzig: H. Kornfeld, 1930.

It is one of the failings of the otherwise so wholesome American tendency to give a prominent position to common sense experience in psychiatry that it is apt to lead to a neglect of the systematized fundamentals of psychiatry in nosological terms. Wittermann gives in concise presentation a combination of strict and unflinching allegiance to classificatory nosology and the practical points apt to figure at the beginning of the various disorders. One cannot help feeling that the student or physician who has mastered the successive discussions of the "diseases" has covered the field systematically. If there were an equivalent of "Living Age in Medicine," this presentation would deserve to appear in English garb.

First symptoms often are mistaken for causes and vice versa. The beginnings are usually slow but often latent, so that a flare-up is apt to be taken as an acute onset. The first issues are the dangers to others and much more frequently to self, and the fact that radical therapy with fevers and occupational training can as a rule be carried out only in an institution. Studies on heredity and the determination of Kretschmer's types of constitution are helpful, but require caution in the deductions for the individual case. A physical examination is obligatory in all cases, and can sometimes give one the only available evidence of dissimulated emotion. A diagnosis of a somatic-infectious delirium should not make one underrate the risks of suicide. On the other hand, Wittermann warns against using debatable observations and methods (Abderhalden) or unproved deductions in court.

He discusses oligophrenic disorders (idiots, imbeciles, debility, amaurotic and mongoloid idiocy, and cretinism, juvenile dementia paralytica, intelligence defects). Then comes the dementia paralytica of the adult, sometimes found at autopsy without adequate clinical symptoms. The early symptoms call for tests of the blood and spinal fluid ("nearly always positive"); arteriosclerosis with its pseudoneurasthenic precursors, and Pick's disease, Alzheimer's disease and the senile disorders.

Concerning epilepsy, Wittermann is cautious and fully aware of the occasional difficulty. The alcoholic psychoses (dipsomania, and chronic alcoholism, delirium tremens, hallucinosis, jealousy, Korsakoff) and also morphinism and cocainism are fully considered. In schizophrenia he follows Kraepelin (unintelligible acts, poor contact, marked egocentricity with hallucinations and abstruse delusions), but gives too little attention to the precursors. Manic-depressive psychoses, more intelligible to the normal person, not necessarily with Kretschmer's types, occur also in mixtures of depression and elation; and patients with hypomania as well as those with depressive states should be institutionalized as a rule. Psychopathic personalities and psychopathics "cannot be considered as Geisteskranke," but they may show psychotic episodes and disharmonies. Early recognition will help much in the guidance of both youngster and parents.

It is interesting, and even refreshing, to see such a discussion without talk about mental hygiene.

METHODEN DER KONSTITUTIONELLEN KÖRPERBAUFORSCHUNG. By FRIEDRICH VON ROHDEN. (Handbuch der biologischen Arbeitsmethoden, Abt. IX, Methoden der Erforschung der Leistungen des tierischen Organismus, Teil 3, Heft 4, Methoden der Vererbungsforschung.) Price, 10 marks. Pp. 173. Berlin: Urban & Schwarzenberg, 1929.

The realities and actualities of man cannot be telescoped into the type of simplicity of even a complex machine without one's losing essential facts or aspects. Yet it is the wish and hope of a certain type of science to attain at least maximal unification. The most fundamental science of man will aim at a reduction of life to physics and chemistry. Since the attention of investigators has spread again from the elements, the cells and the individual organs to the organisms as a unit, there has arisen a desire to systematize the lasting properties of the individual and a revival of study which is a great advance beyond the temperaments, the

physiognomic character readings, the horoscopes, the graphology, the types of degeneracy or the more or less nosological types, viz., to the types of statural proportions.

The present study is part of the volume on studies of heredity dealing with typology. In an historical outline and table are 34 groupings, of which 22 rest on a 3-type or more and 12 on a 2-type scheme. In the main, one recognizes as a generally acceptable upshot the leptosomic and pyknic and the intermediate athletic type singled out by Kretschmer as the most useful contrasts. A general part deals with a critique of the methods, especially also of Kretschmer's principle, and the methods of classifying and comparing the types. The special part (following the 50 pages of the general part) gives in about 120 pages a full survey of the morphology of the tissues, the study of the forms of head, body and viscera, the somatometric methods, the statistical methods in use and the means of presentation of the results.

Of American literature, the work of Wertheimer (Wertham) and Hesketh receives full utilization. The study of Lewis on the visceral constitution of schizophrenic patients and the studies of Draper are not included, although they should at least be considered as variants also calling for some attention for research on heredity. For methodological orientation the review deserves to be called an obligatory source of orientation.

SOME SOCIAL ASPECTS OF MENTAL HYGIENE. Edited by FRANKWOOD E. WILLIAMS. Part 3 of Volume 149 of the Annals of the American Academy of Political and Social Science. Price, $1. Pp. 214. Philadelphia, 1930.

This volume is a collection of papers dealing with phases of the sociologic application of the principles of mental hygiene. The table of contents indicates the various topics covered: Part I. General Aspects: Finding a Way in Mental Hygiene, by Frankwood E. Williams. Eugenic Sterilization in the United States: Its Present Status, by Frederick W. Brown. Mental Hygiene in Preventive Medicine, by William L. Russell. The Runaway Child: A Case Study, by Florence Gilpin. Social Adjustment of the Feeble-Minded, by Florence Powdermaker. The Social Significance of the Psychopathic, by Karl Birnbaum. Pooling and Coordination of Effort in Mental Hygiene Clinics, by E. Van Norman Emery.

Part II. Mental Hygiene in Education and in Mercantile Life: Mental Hygiene from the Standpoint of College Administration, by Charles D. Bohannan. Causes of Mental Ill Health Among College Students, by George E. Gardner. The Contribution of Psychiatry to Some Educational Problems, by Mandel Sherman. The Mental Health Value of Special Education, by Edgar A. Doll. The Public School and the Problem Child, by R. Ray Scott. The Public School and the Mentally Defective Adolescent, by Horace Victor Pike. The Child of Very Superior Intelligence as a Special Problem in Social Adjustment, by Leta S. Hollingworth. The Psychiatric Social Worker in Mercantile Life, by Mary B. Laughead.

Part III. Institutional Treatment and Community Organization: Community Control of the Feeble-Minded, by Edgar A. Doll. Child Guidance Problems in Rural and Village Communities, by Sanger Brown. Mental Hygiene Functions of the Public Health Nurse, by Sybil H. Pease. Mental Diagnosis and Probation, by E. Van Norman Emery. Extra-Institutional Activities of Mental Hospitals, by William C. Sandy. The Follow-Up Service of a Mental Hospital, by Katherine E. Howland.

The quality of the articles, expressing the wide experience of the authors, makes this symposium one that should be of interest and value to educationalists, sociologists, psychiatrists and social workers.

DIE ZENTRALE ABSTIMMUNG DER SEHSPHÄRE. By HANS HOFF. Price, 7.80 marks. Pp. 96, with 7 illustrations. Berlin: S. Karger, 1930.

A patient with traumatic epilepsy had one type of attack at night and a slightly different type in the daytime. "It is possible in this patient to produce day attacks

regularly by means of a subcutaneous injection of 0.03 cc. of cocaine, a drug that has an almost purely cortical point of attack in this concentration." By means of cardiazol, which, according to Schön, "has its point of attack in the region of the center producing sleep, night attacks were always produced . . . thus, one sees by analysis of the mechanism of this attack that the state of the visual sphere is regulated by that deep apparatus the function of which it is to preside over the periods of sleeping and waking."

Medinal, paraldehyde and atophanyl were administered to apparently normal persons to observe the effects produced on their dreams. "The dreams following the use of soluble barbital and paraldehyde were marked by a usual liveliness and the appearance of many small objects . . . I attempted by atophanyl, which according to Wermer and myself has its action on the cortex, to influence this center in order to study the effect on sleep. My subject received, therefore, 10 cc. of atophanyl intravenously before going to sleep. The dreams of these patients were constant. For the most part the feeling of strangeness which characterizes these dreams — curious towers in bizarre forms and colors, deep gullies, water, peculiar, large oddly moving men — would be seen in them. . . . One sees, therefore, that alteration in the region of the thalamus markedly influences the dream content."

Among other conclusions, one finds that "the center of the regio interparietalis has the function to conduct stimuli from the sense sphere, to protect visual spheres by means of denervation of injurious influences, and finally to transmit stimuli in a certain direction, to distribute them and to insure praxia."

These brief selections taken at random illustrate the type of observation and deduction in this monograph, which scarcely merits further description.

THE PSYCHIATRIC STUDY OF PROBLEM CHILDREN. By SANGER BROWN II and HOWARD W. PORTER. Pp. 152. Utica, N. Y.: State Hospitals Press, 1930.

This monograph, published by the New York State Department of Mental Hygiene, is (as the authors state in the preface) an attempt to present a general outline of the methods approved by qualified workers for the examination of children who present psychiatric problems. It is divided into three parts. Part 1 deals with the methods employed in the study of the patient — physically, biochemically, psychologically and psychiatrically — and the environment to which he is and has reacted. Part 2 describes clinical types of problem children. The authors have classified these into five types: (1) with physical etiologic factors, (2) with mental deficiency, (3) with other variations in intelligence, (4) with other mental and environmental causes and (5) behavior disorders. Part 3 is devoted to the question of treatment.

The book is intended as an outline of examination methods and as such it should be of value to physicians, psychologists, social workers and others who attempt to familiarize themselves with methods of examining children with psychiatric problems. Like outlines in general, however, its space is too limited to present many important factors adequately. Too much space is devoted to considerations of physical conditions and mental defect — the chapter on the latter is very good, however — and too little is devoted to a consideration of the emotional attitudes in the family and their highly important effect on the child's personality and behavior. The section on "nervousness" should be deleted from subsequent editions; it tends to give a misleading and inaccurate impression through its apparent emphasis on physical causes and shocks which are rarely encountered as true etiologic factors. Nor does it seem necessary in such a volume to discuss in a controversial manner the extremely valuable contributions of psychoanalysts.

The appendix contains synopses and forms which will be helpful to the student in arranging and recording data.

Used in the manner intended by the authors — as a guide to the examination and study of psychiatric problems of children — this little book should prove of great value to all who work with problem children and particularly to those just entering this field.

MEDIZINISCHE PSYCHOLOGIE. By DR. ERNST KRETSCHMER. Fourth edition. Price, 16 marks. Pp. 266. Leipzig: Georg Thieme, 1930.

This edition of Kretschmer's "Medical Psychology" (first published in 1920, with the third edition in 1926) discusses the psychic "fundamental functions" and the anatomic physiologic synthesis, the psychic mechanisms and their evolutionary synthesis, the instincts and temperaments, the personalities and reaction types and practical medical psychology—a not altogether simple and lucid progression. The book presents largely the general conceptions current in German teaching, but with all the contributions for which Kretschmer is known, and with good surveys of such studies as those of the Jaensch school and the studies with mezcaline, and the cerebral localizations. On the other hand, he gives full space to the psychologic topics reaching into the field of the hypnotic and dream experiences and the hypobulic mechanisms, panic, etc. Throughout there is a judicious recognition of a wide range of facts accredited to Freud, but clearly digested in Kretschmer's own experiences and with relative freedom from dogmatism. In his discussions of "psychoanalytic methods" he is definitely unorthodox, without, however, becoming a mere irresponsible eclectic.

The presentation as a whole still makes somewhat heavy reading. It is difficult to bring the wide field into groups of statements that are not either too broad or too narrow. Schilder's book shows a similar difficulty. The best effort in this direction seems to the reviewer to be the Norwegian book by Ragnar Vogt. It is an interesting question which one of the available books would be most welcome to American students. Kretschmer's would no doubt be a valuable and stimulating help in a judicious English translation with a certain easing up and pointedness and a gain in clarity of the arrangement. The German text should, however, not be too difficult to one with a reasonably fair start in reading knowledge.

DIE EXPERIMENTELLEN GRUNDLAGEN DER EIERSTOCKSVERPFLANZUNG. By A. LIPSCHÜTZ. Price, 3 marks. Pp. 73, with 10 illustrations. Budapest: Rudolf Novak & Company, 1930.

This monograph brings the author's excellent book, "The Internal Secretions of the Sex Glands," 1924, up to date. The success of ovarian transplantation differs in different species of animals. With proper technical precautions, almost 100 per cent of takes may be attained with homotrasplantations in the guinea-pig, even when the ovary is transplanted into a male. On the other hand, the proportion of success in rabbits is very small. In guinea-pigs, about 70 per cent of the successful takes are apparently still functioning after nine months. The animals receiving the transplants cannot be said to return to complete sexual normality. Heterotransplantations have never been anatomically proved successful, although it is possible that in the process of absorption they may yield hormones. It is not certain whether primary follicles appear in the transplanted ovary. Ovary preserved on ice may take root and grow, but the proportion of failures steadily increases as time goes on; thus only five of twenty-one experiments were successful in which the ovary was preserved on ice for from seven to sixteen days. The same may be said of drying.

Further details should be read in the original, but it is clear from what has been said that the present outlook of transplantation of endocrine glands for clinical purposes is not good.

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